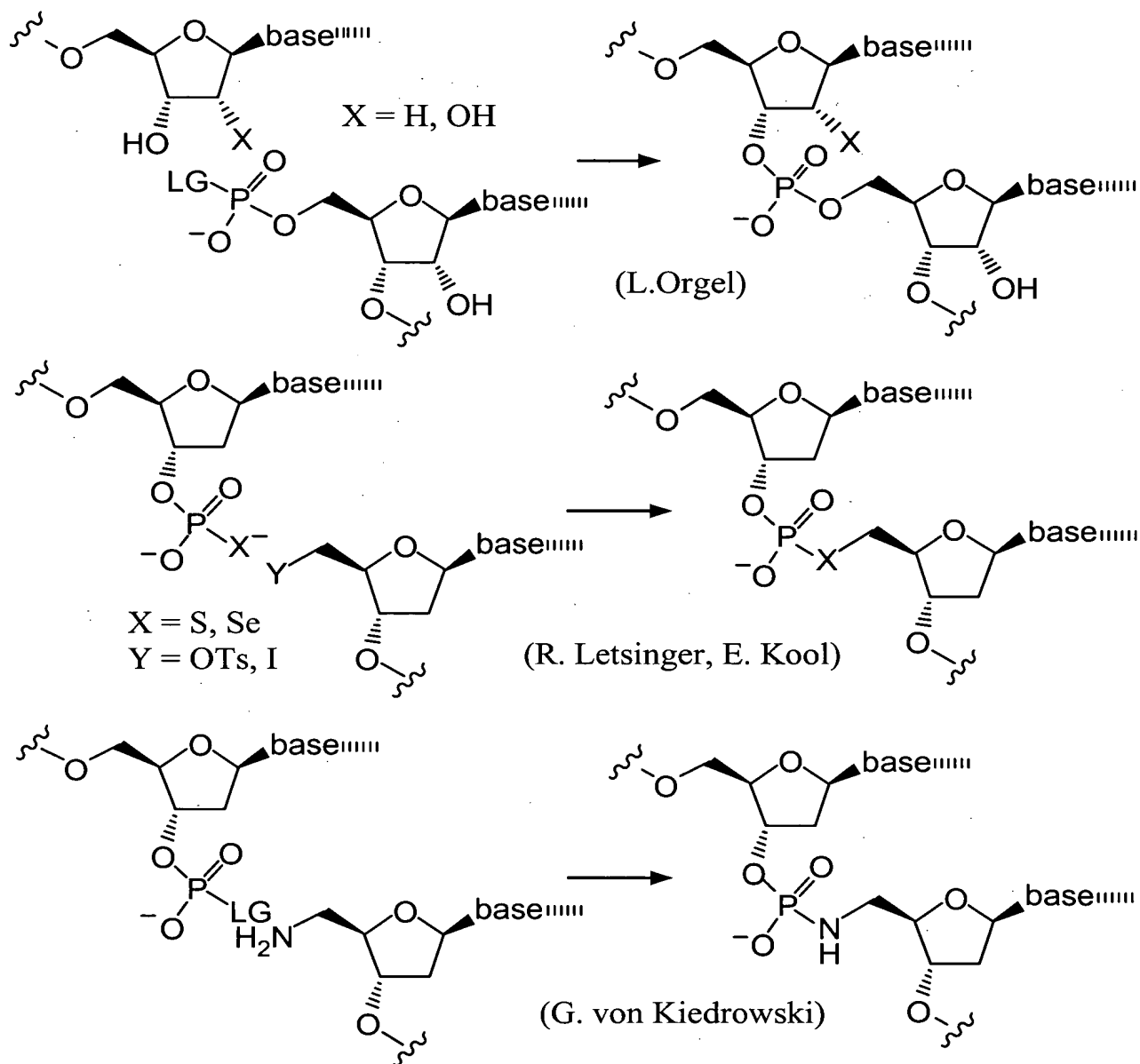




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|         |         |
|---------|---------|
| FIG. 1A | FIG. 1B |
|---------|---------|

FIG. 1

FIG. 1A

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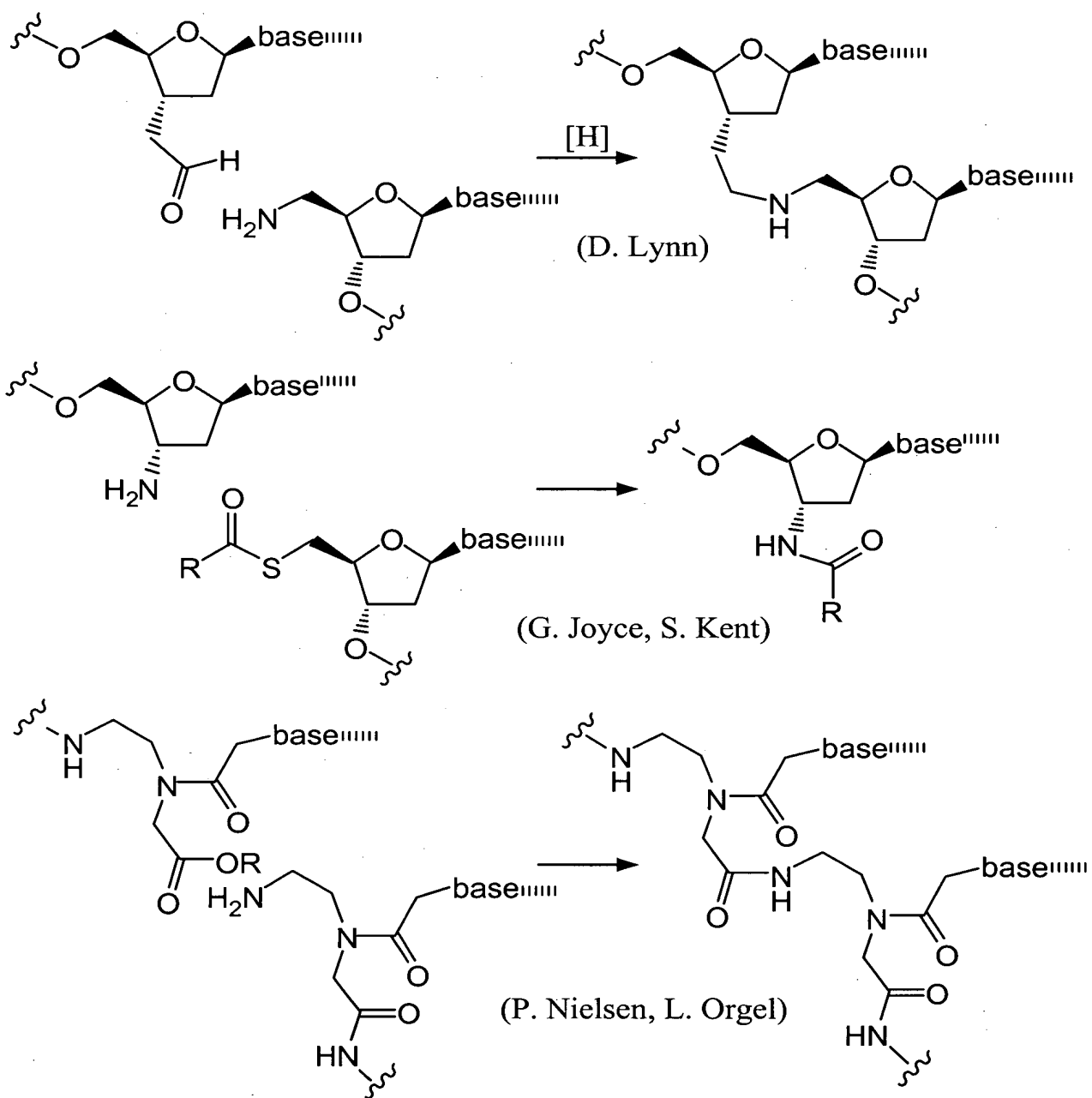


FIG. 1B

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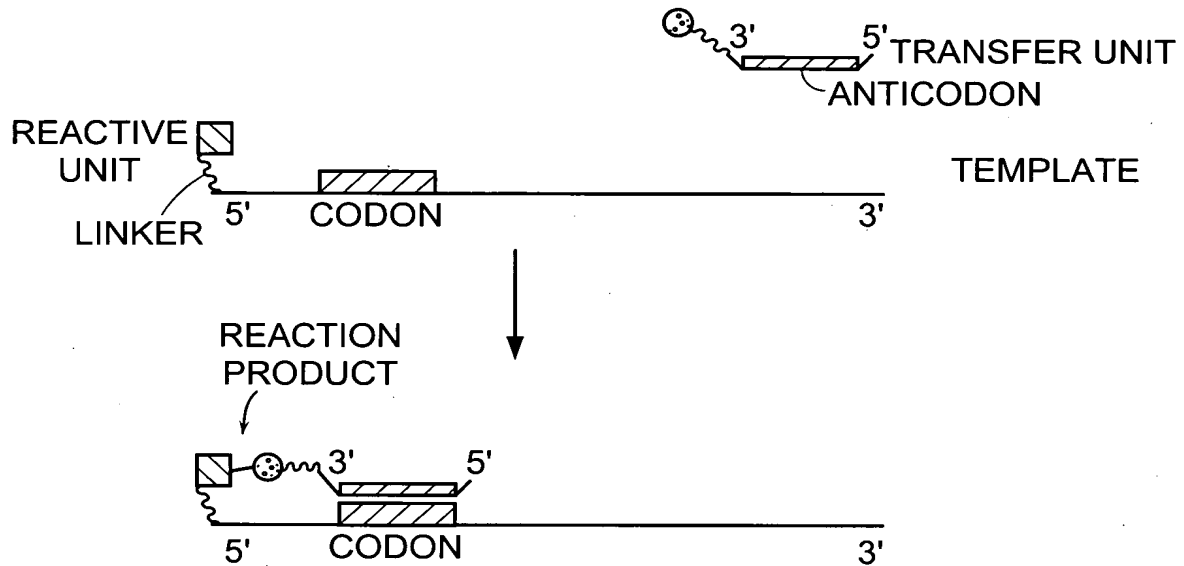


FIG. 2

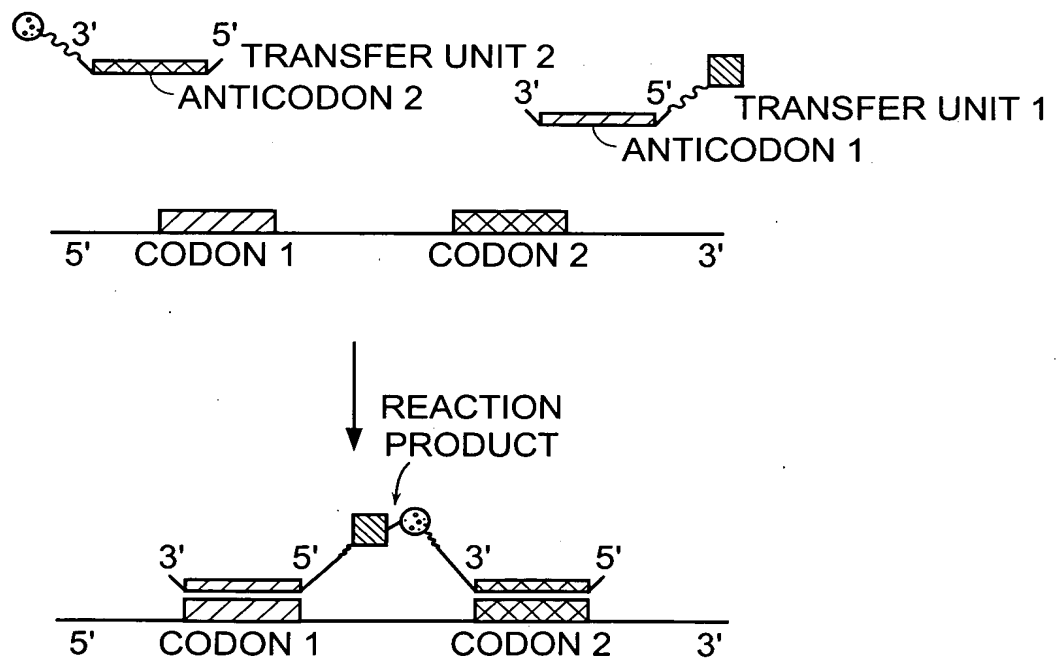


FIG. 3

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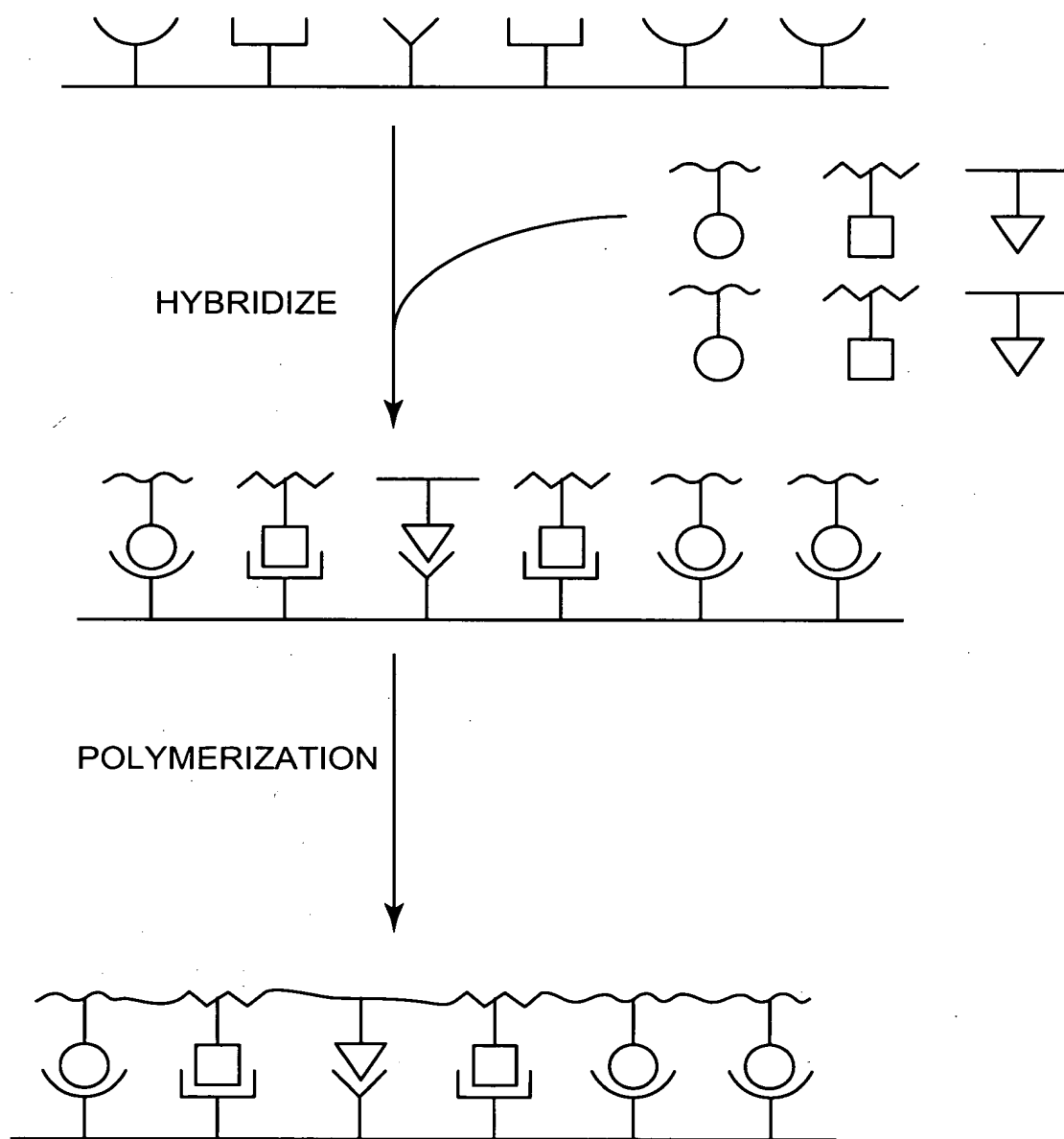


FIG. 4

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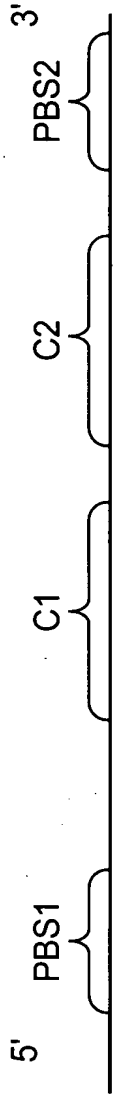


FIG. 5A

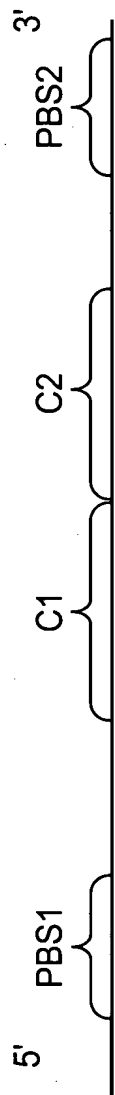


FIG. 5B

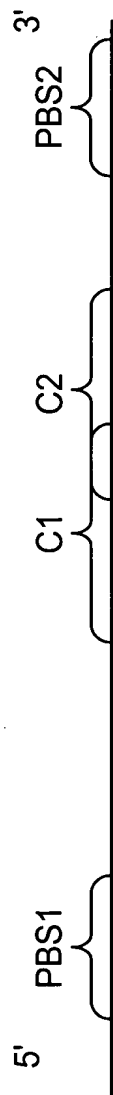


FIG. 5C

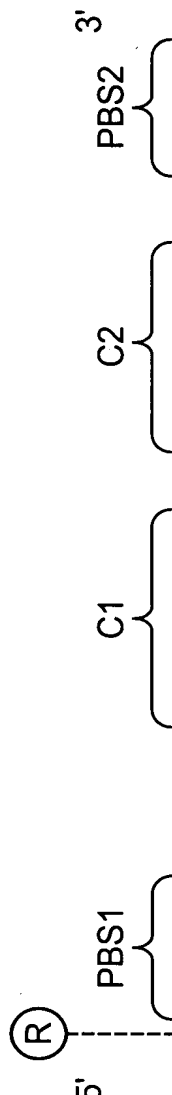


FIG. 5D

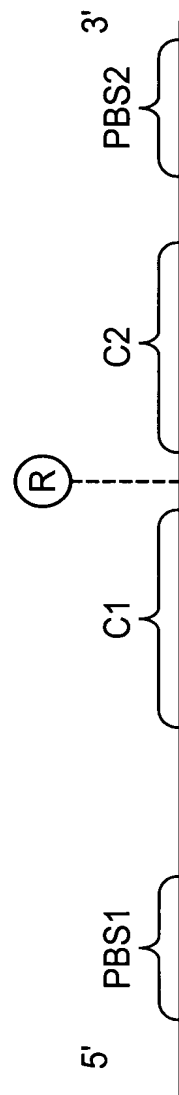


FIG. 5E

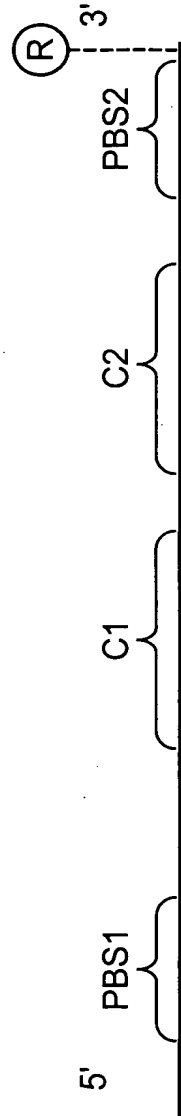
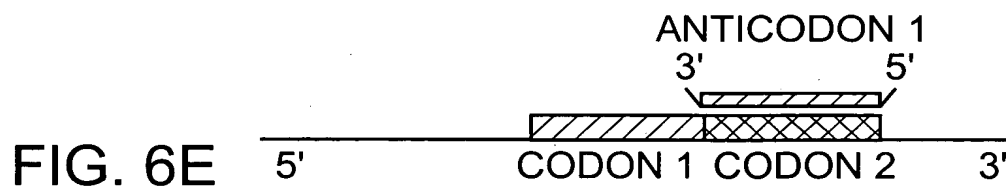
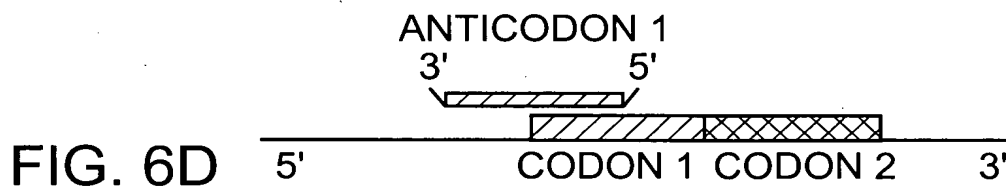
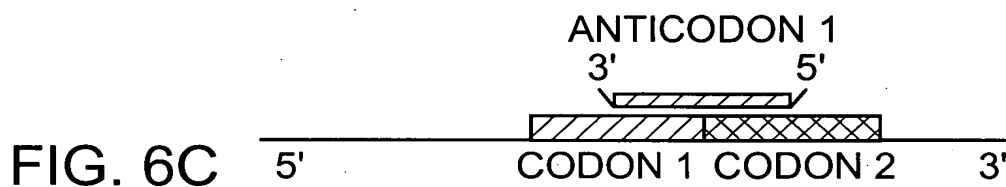
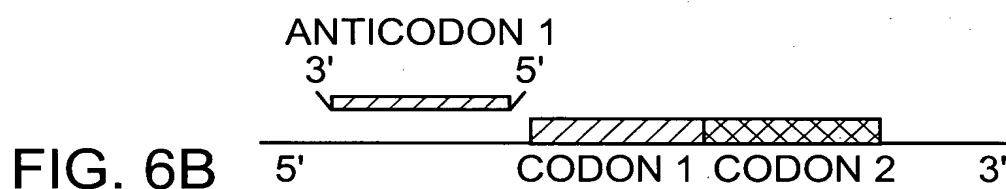
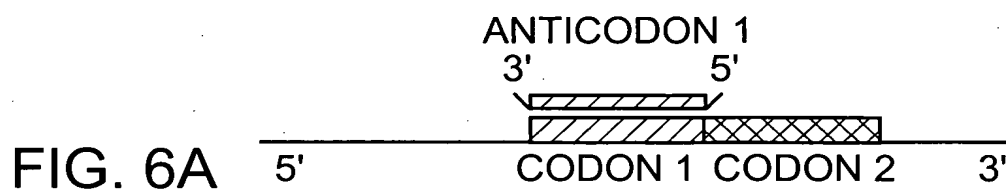


FIG. 5F

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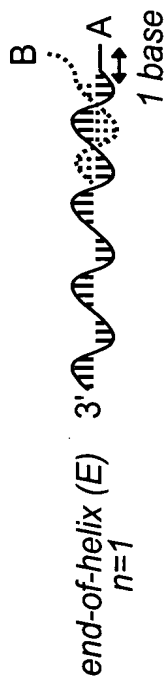


FIG. 7A

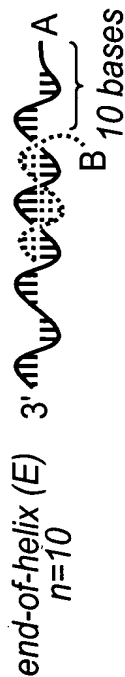


FIG. 7B



FIG. 7C



FIG. 7D

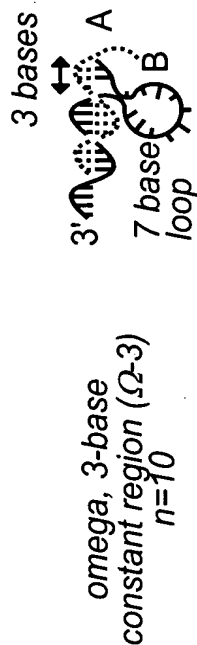


FIG. 7E

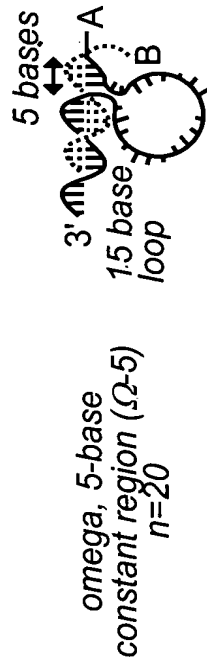


FIG. 7F



FIG. 7G

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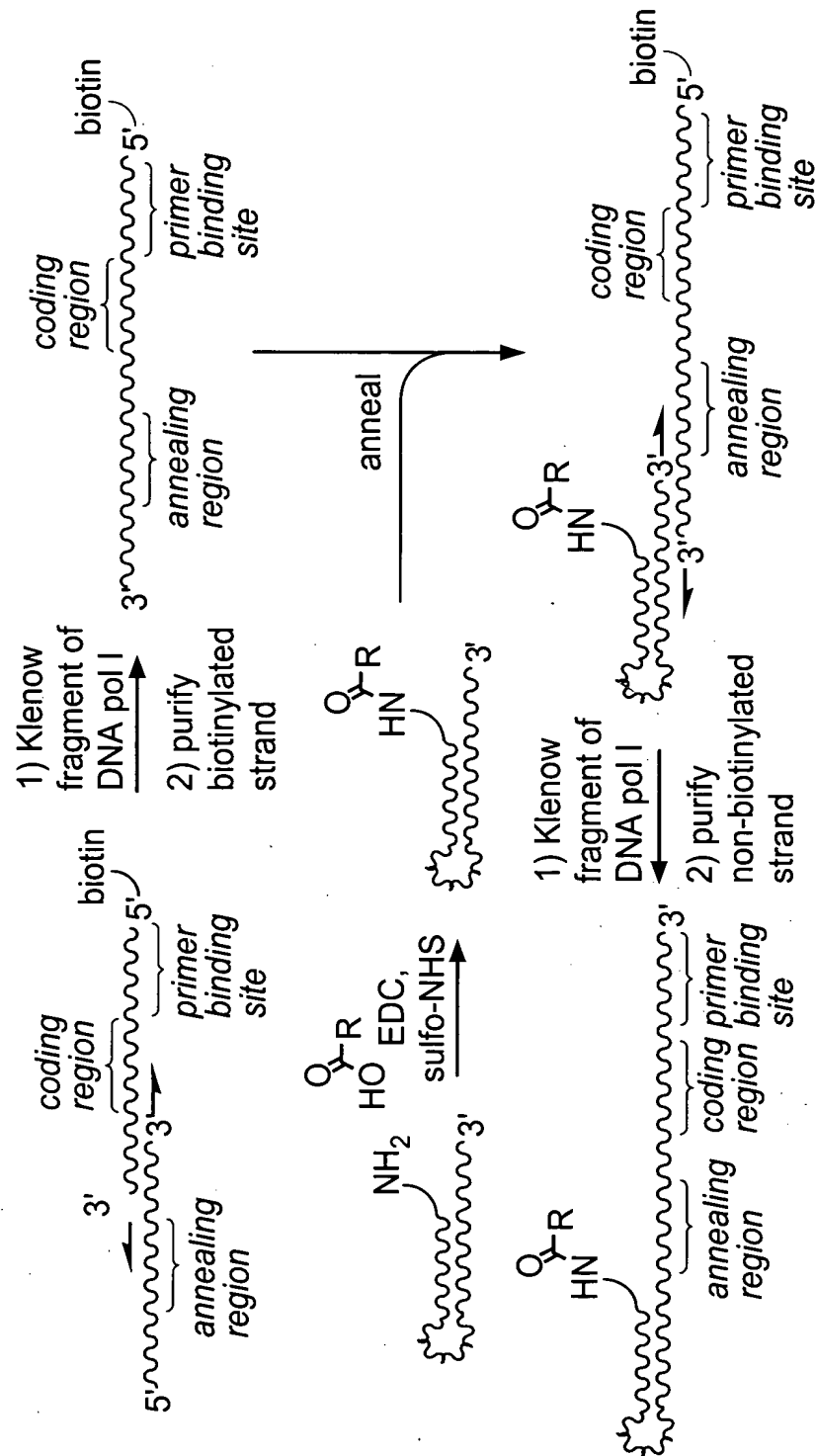


FIG. 8



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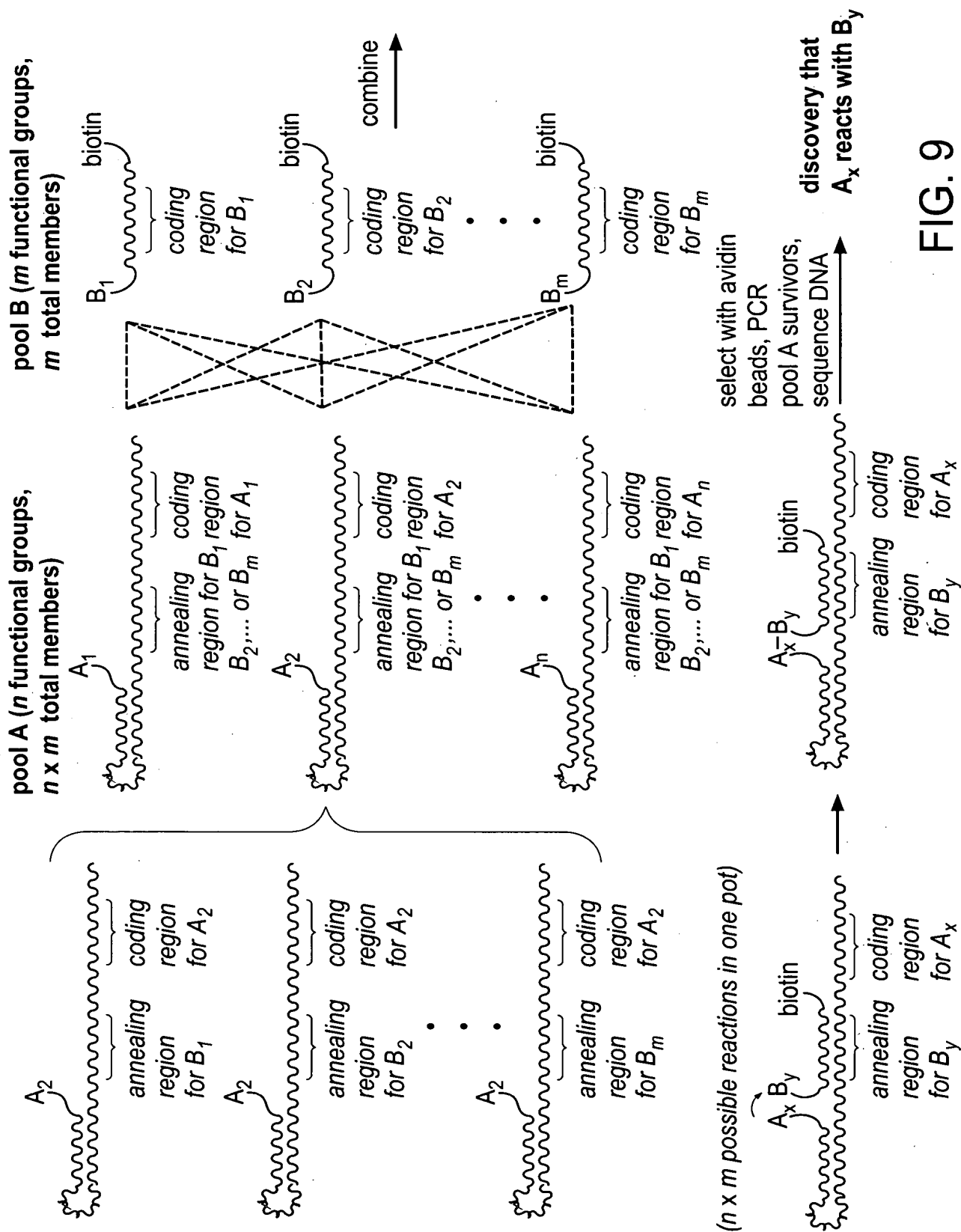


FIG. 9

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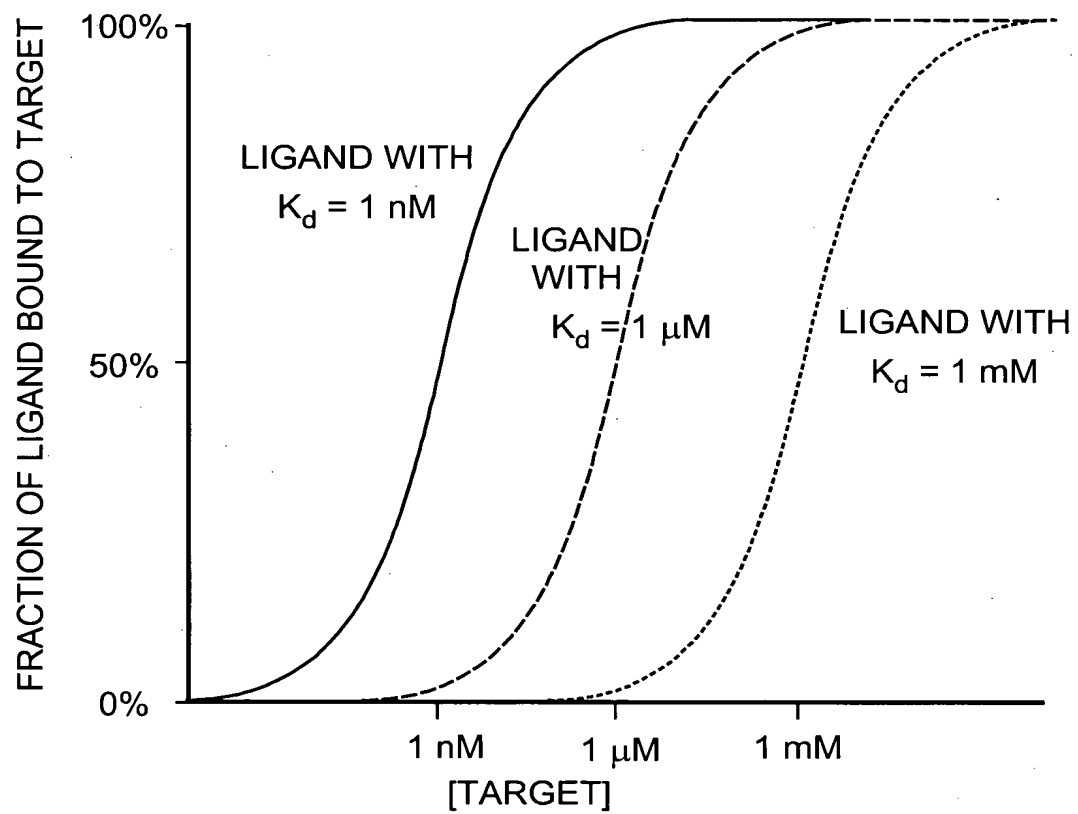


FIG. 10

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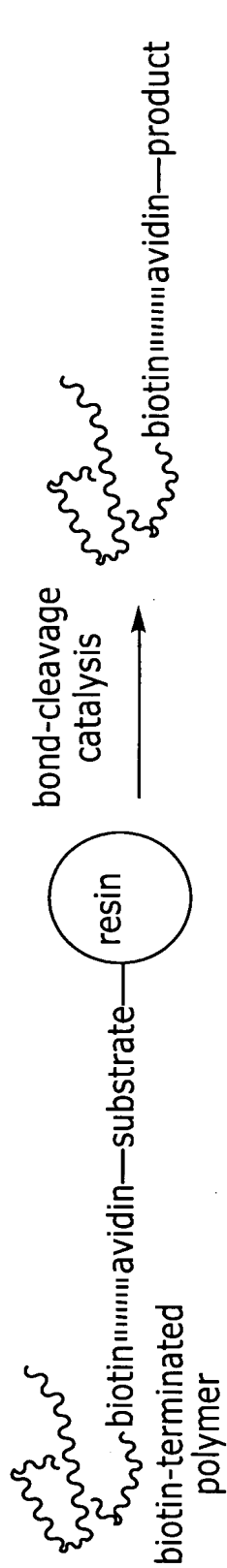


FIG. 11A

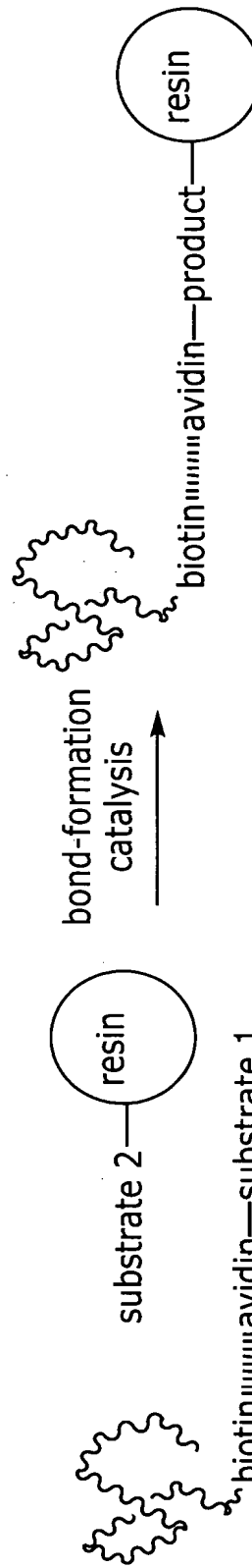


FIG. 11B

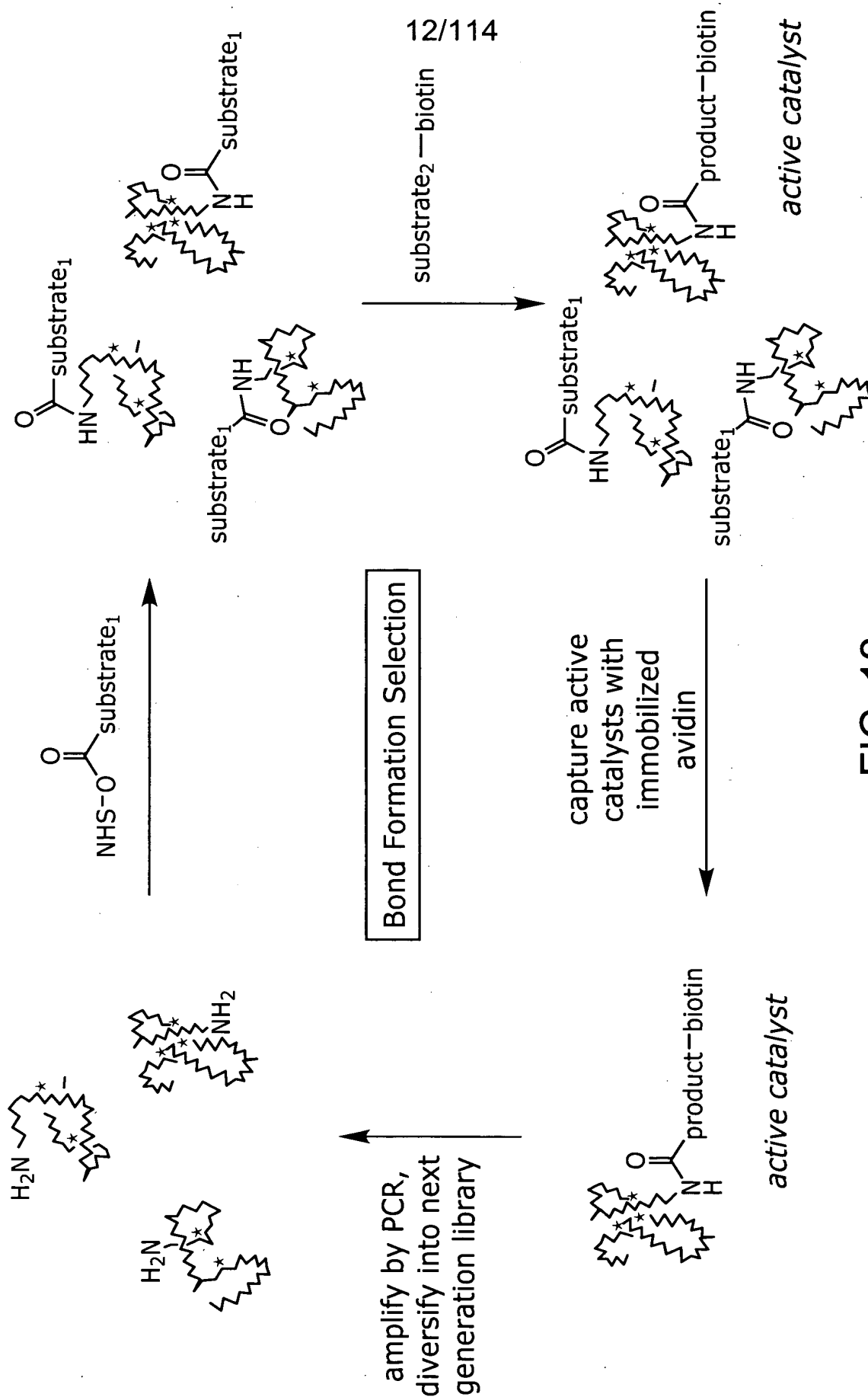


FIG. 12

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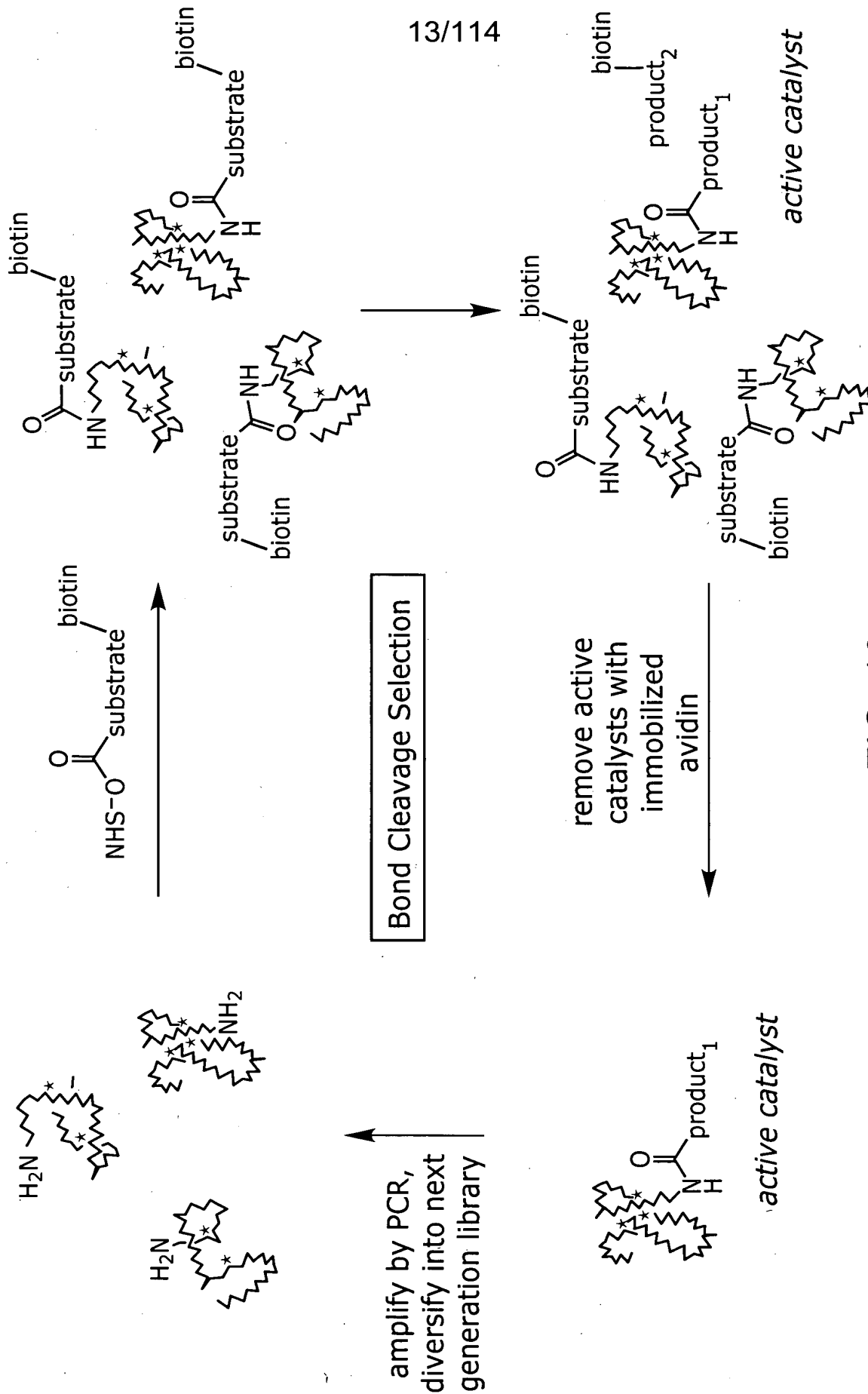
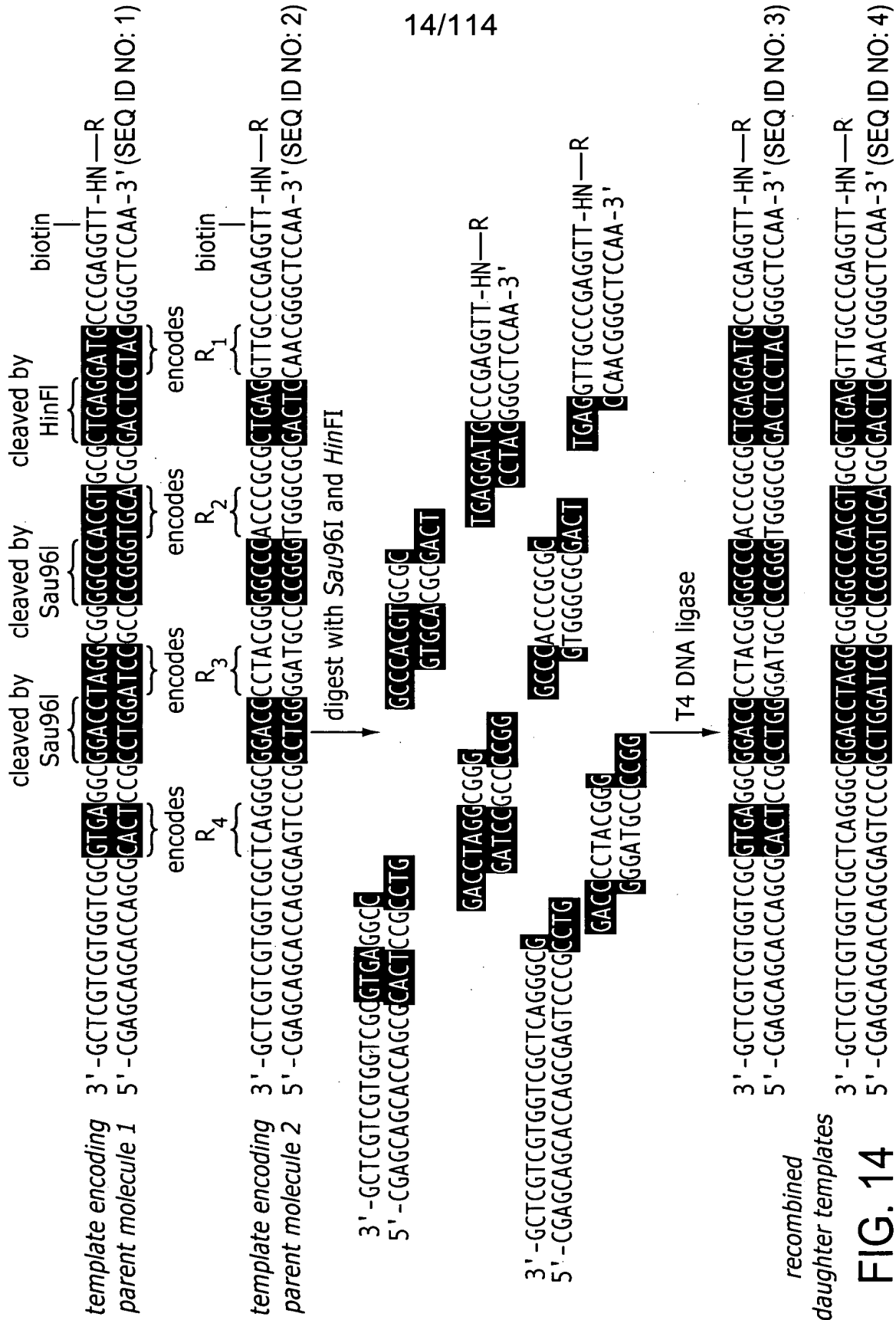
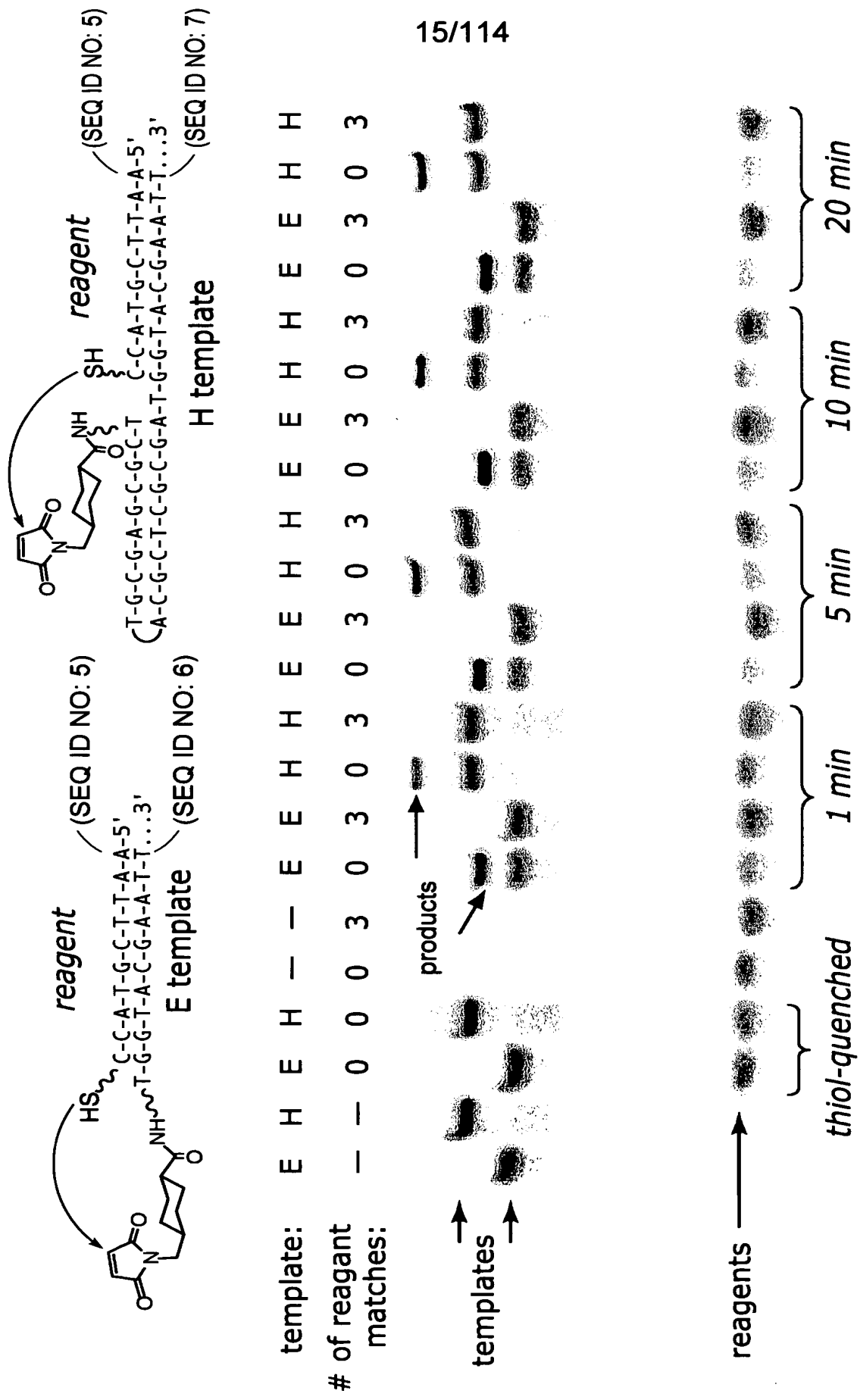
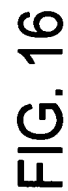
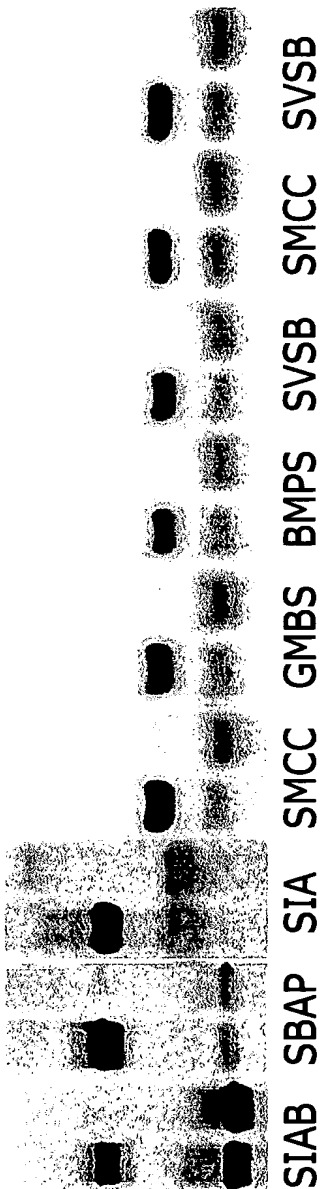


FIG. 13









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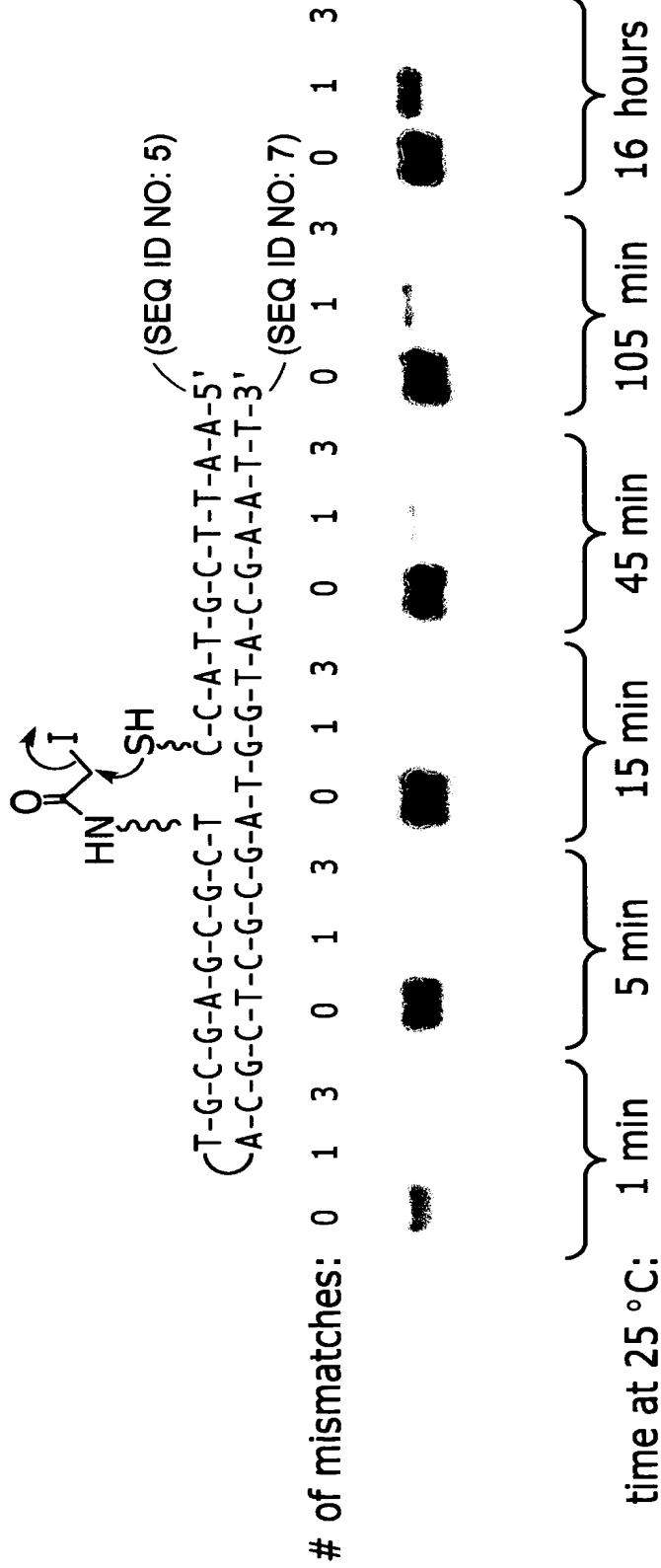


FIG. 17A

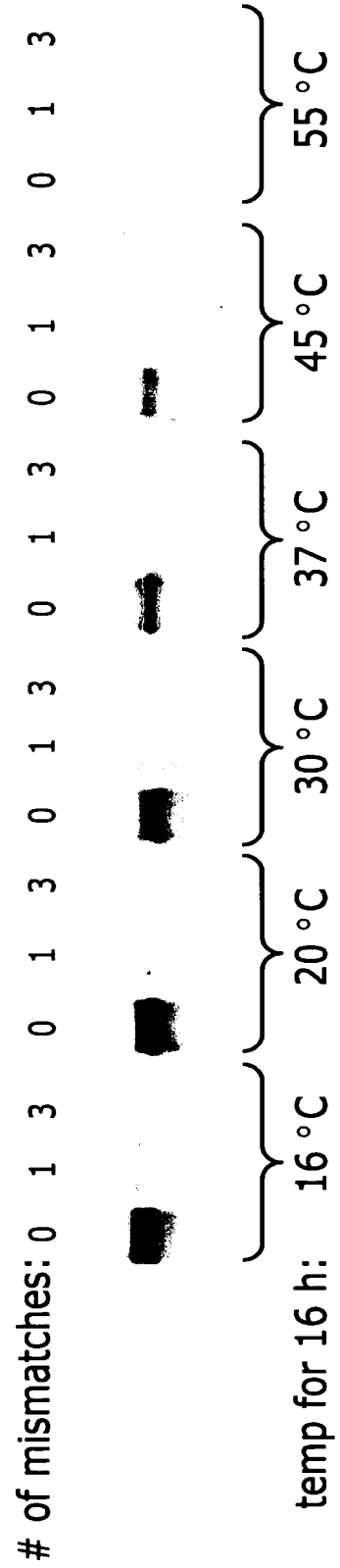


FIG. 17B

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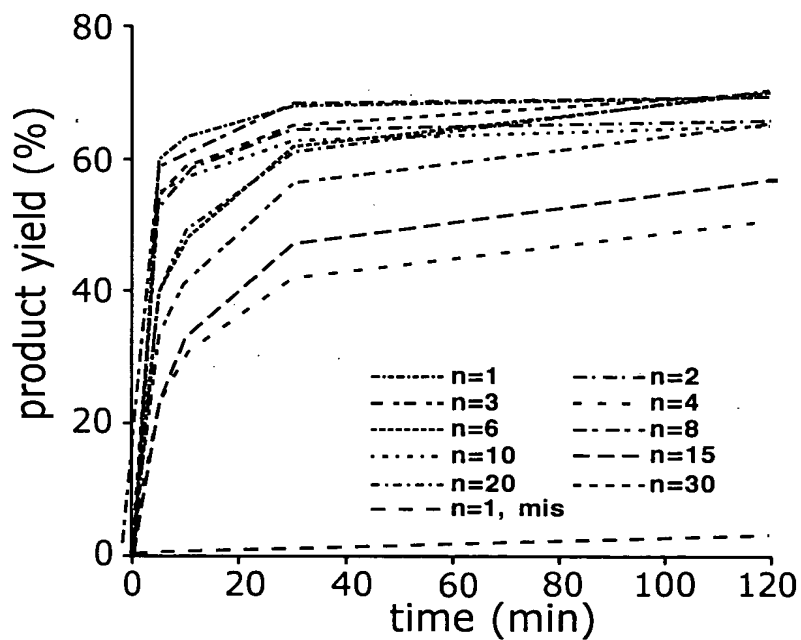
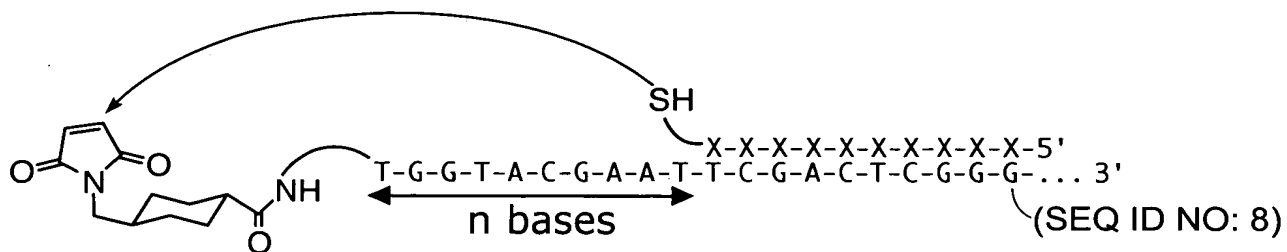


FIG. 18

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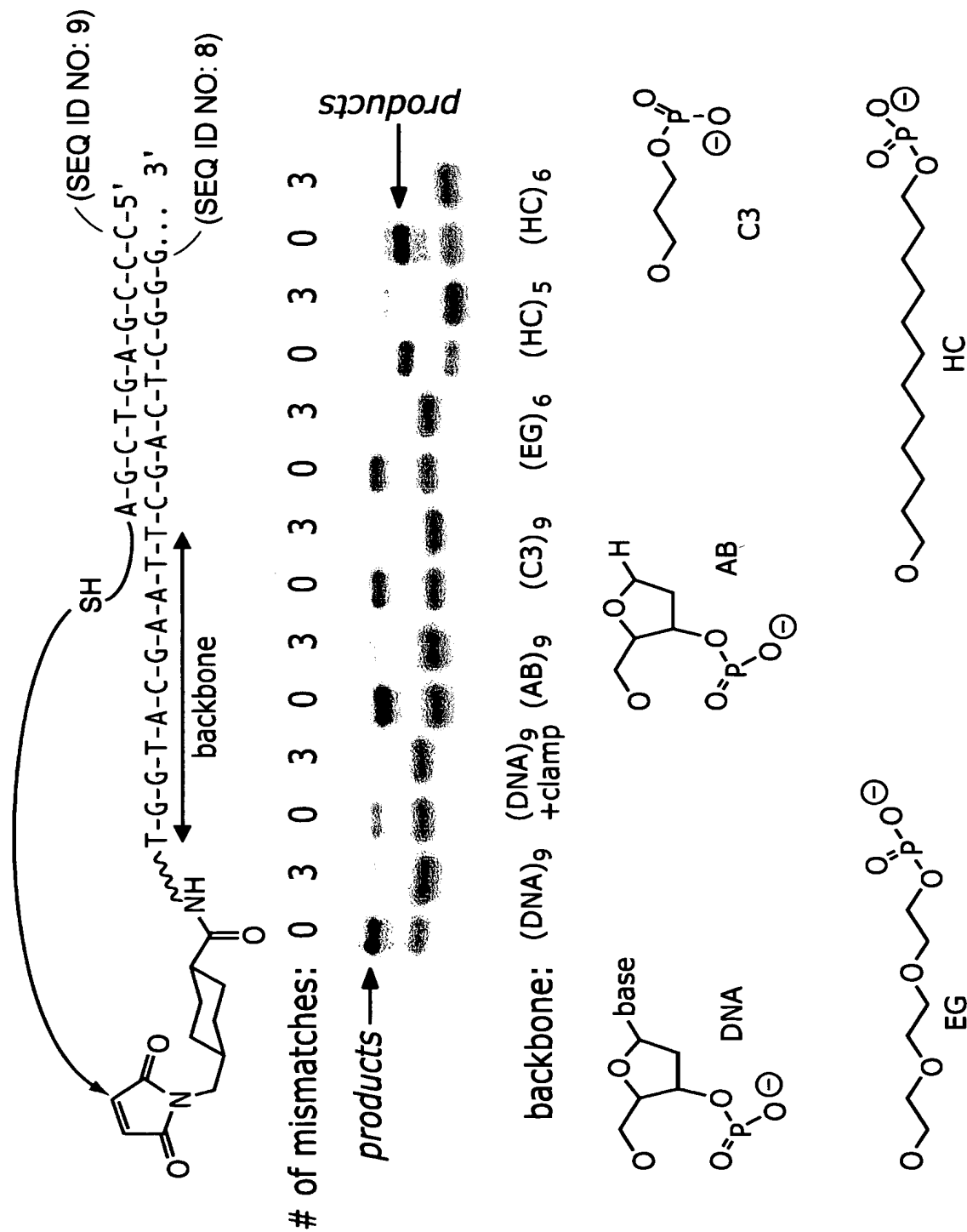


FIG. 19

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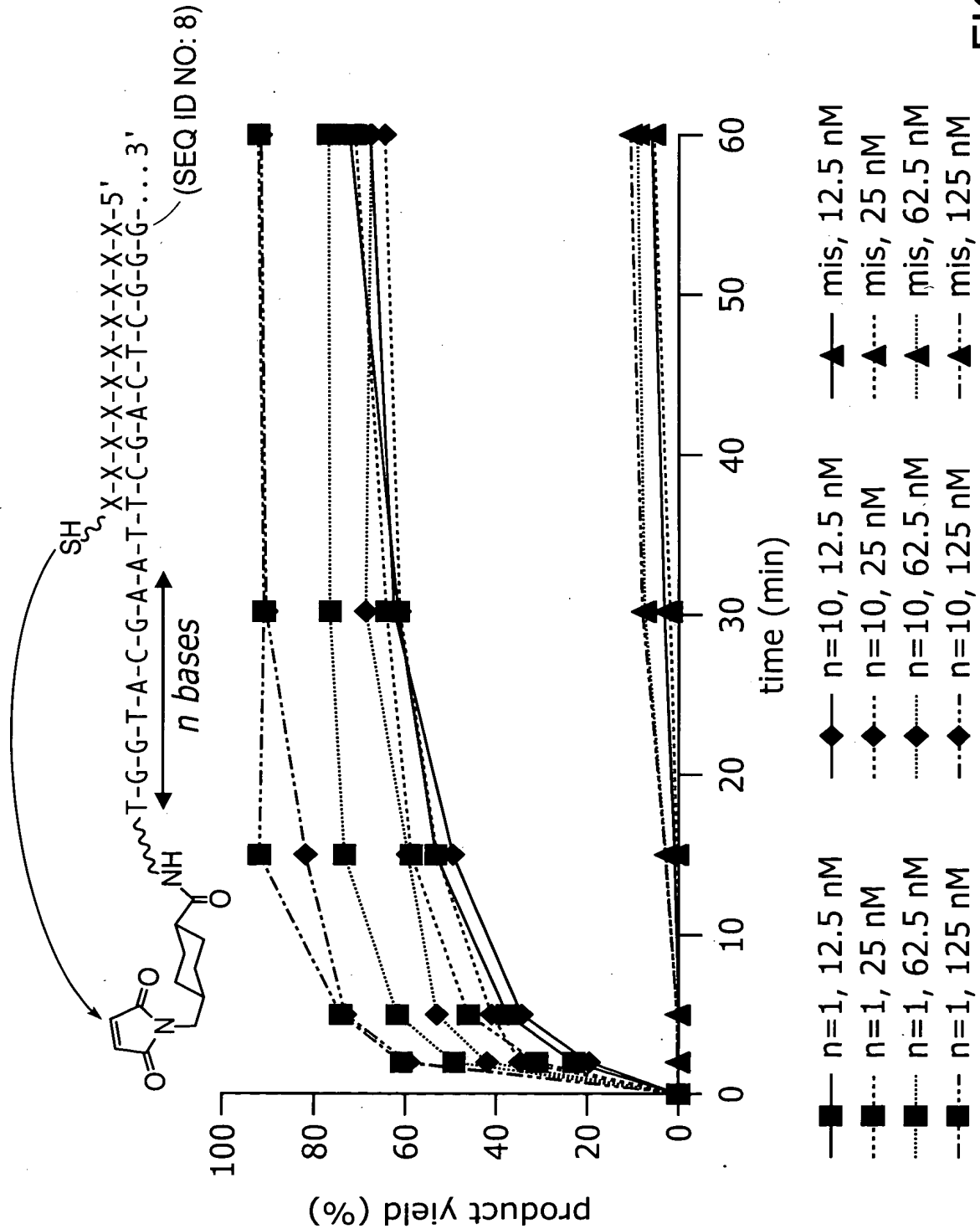


FIG. 20

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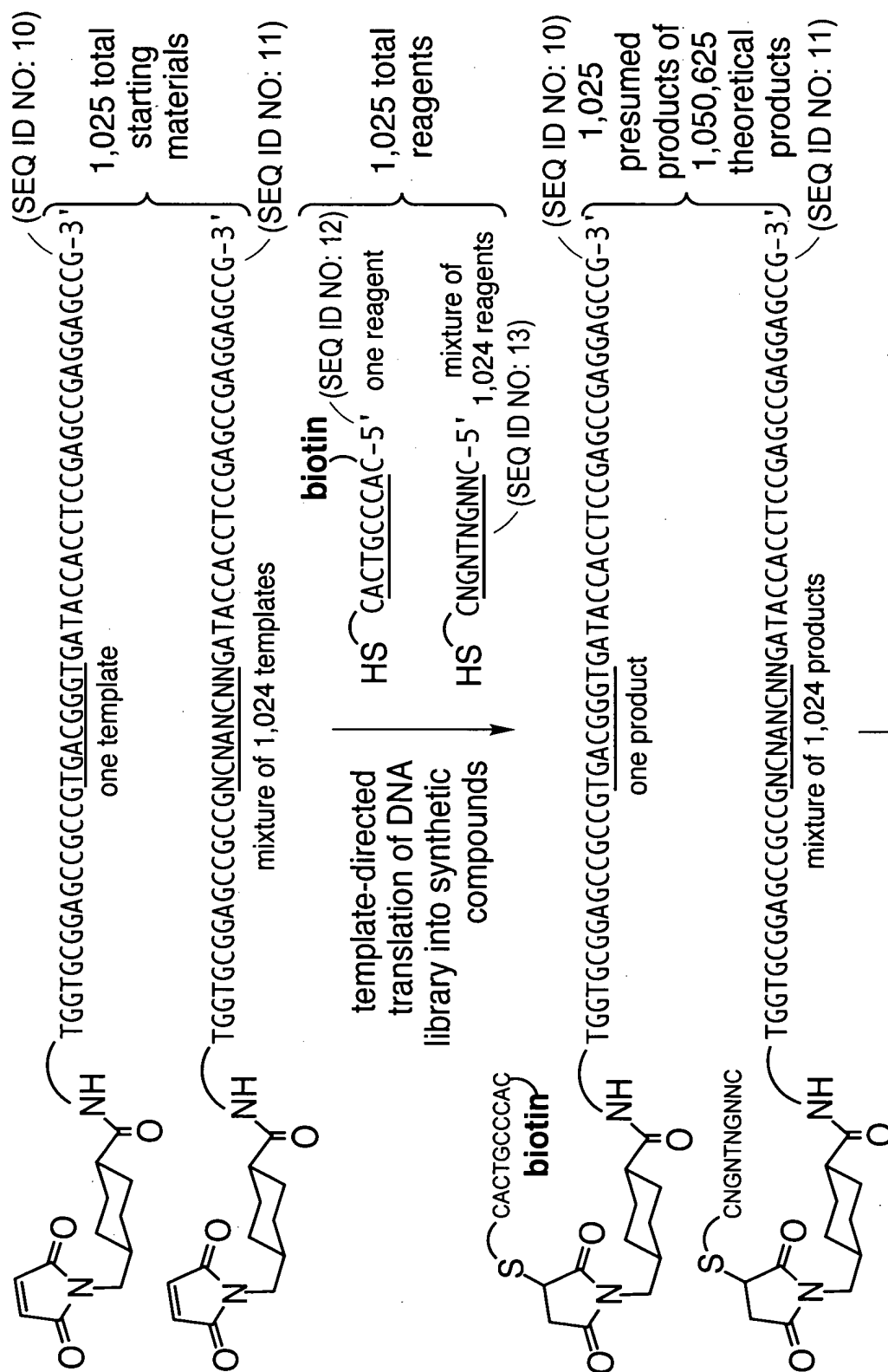


FIG. 21A

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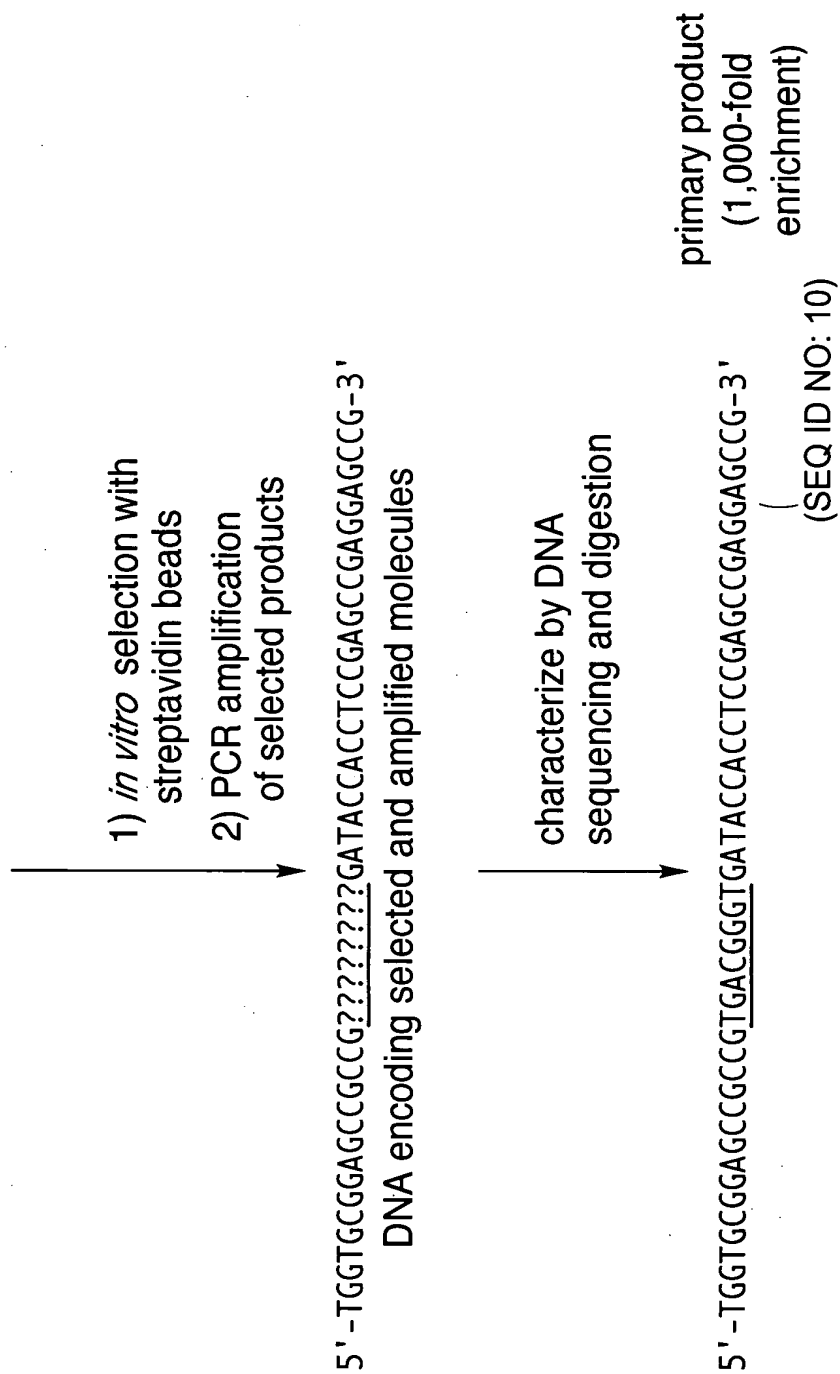
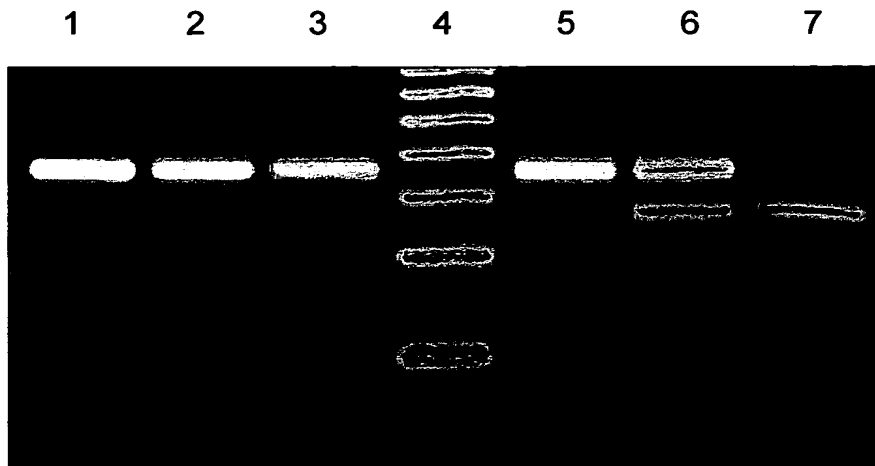
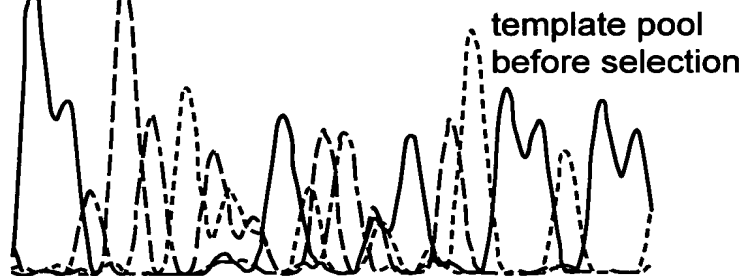


FIG. 21B

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3'---GGT AT CNN G NT NGN C G G C G G--- non-biotin encoding (residues 30-11 of SEQ ID NO: 11)



3'---GGT AT CAC C CGT CAC G G C G G--- biotin encoding (residues 30-11 of SEQ ID NO: 10)

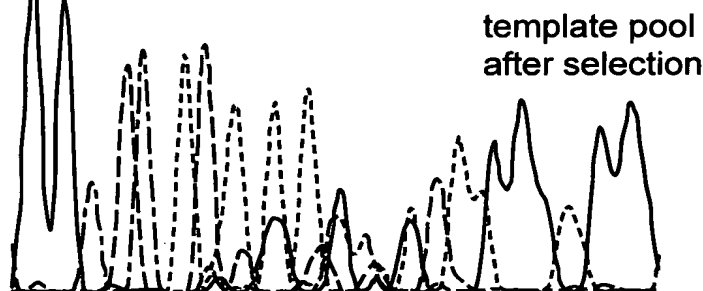


FIG. 22A

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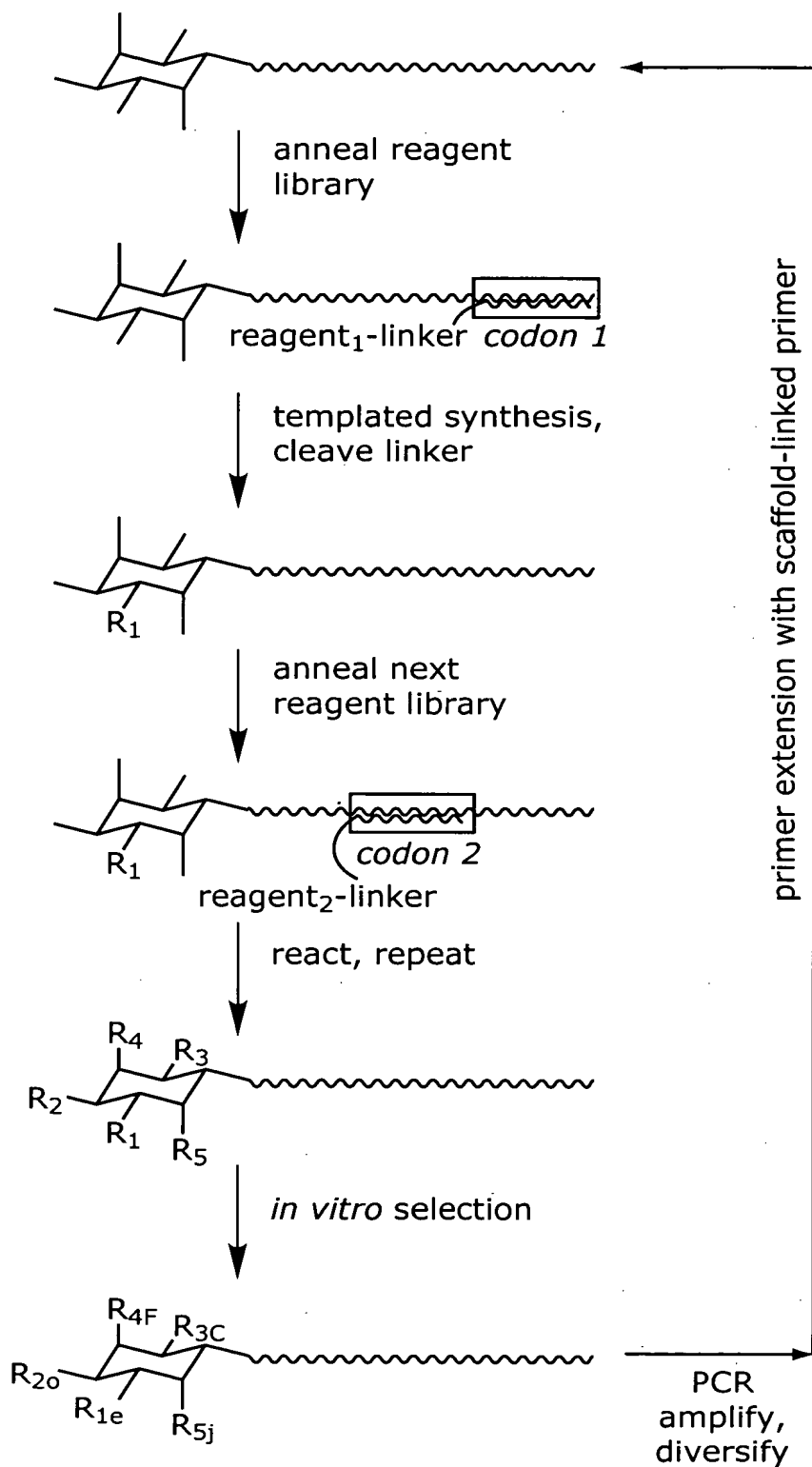
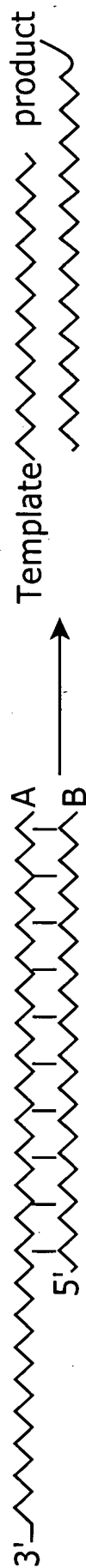


FIG. 22B





| <u>A</u>      | <u>B</u>      | <u>conditions</u> | <u>product</u> | <u>yield (%)</u> |
|---------------|---------------|-------------------|----------------|------------------|
| <br><b>1</b>  | <br><b>2</b>  | a                 | <br><b>81</b>  | 81               |
| <br><b>1</b>  | <br><b>3</b>  | a                 | <br><b>70</b>  | 70               |
| <br><b>11</b> | <br><b>10</b> | b                 | <br><b>45</b>  | 45               |
| <br><b>12</b> | <br><b>10</b> | b                 | <br><b>42</b>  | 42               |

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FIG. 23A

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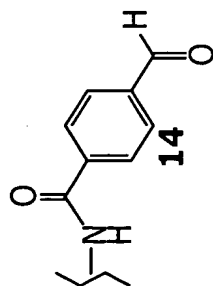
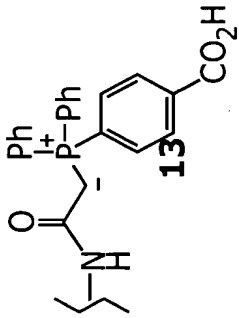
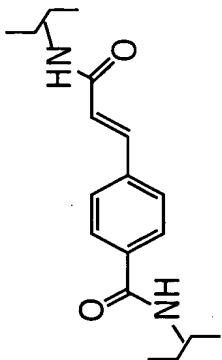
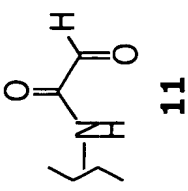
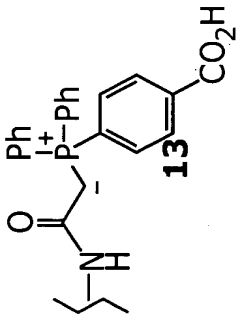
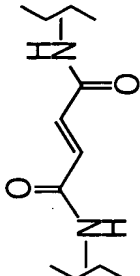
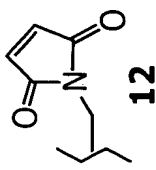
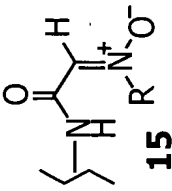
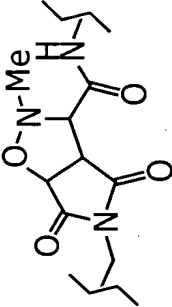
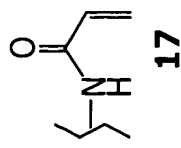
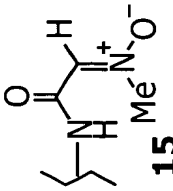
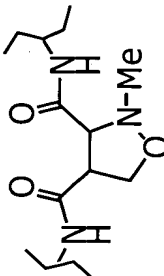
| <u>A</u>  | <u>B</u>  | <u>conditions</u> | <u>product</u>  | <u>yield (%)</u>       |
|---|---|-------------------|---|------------------------|
|    |    | c                 |    | 93                     |
|    |    | c                 |    | >97                    |
|   |   | d                 |   | 53 (R=Me)<br>42 (R=Bn) |
|  |  | d                 |  | 54                     |

FIG. 23B

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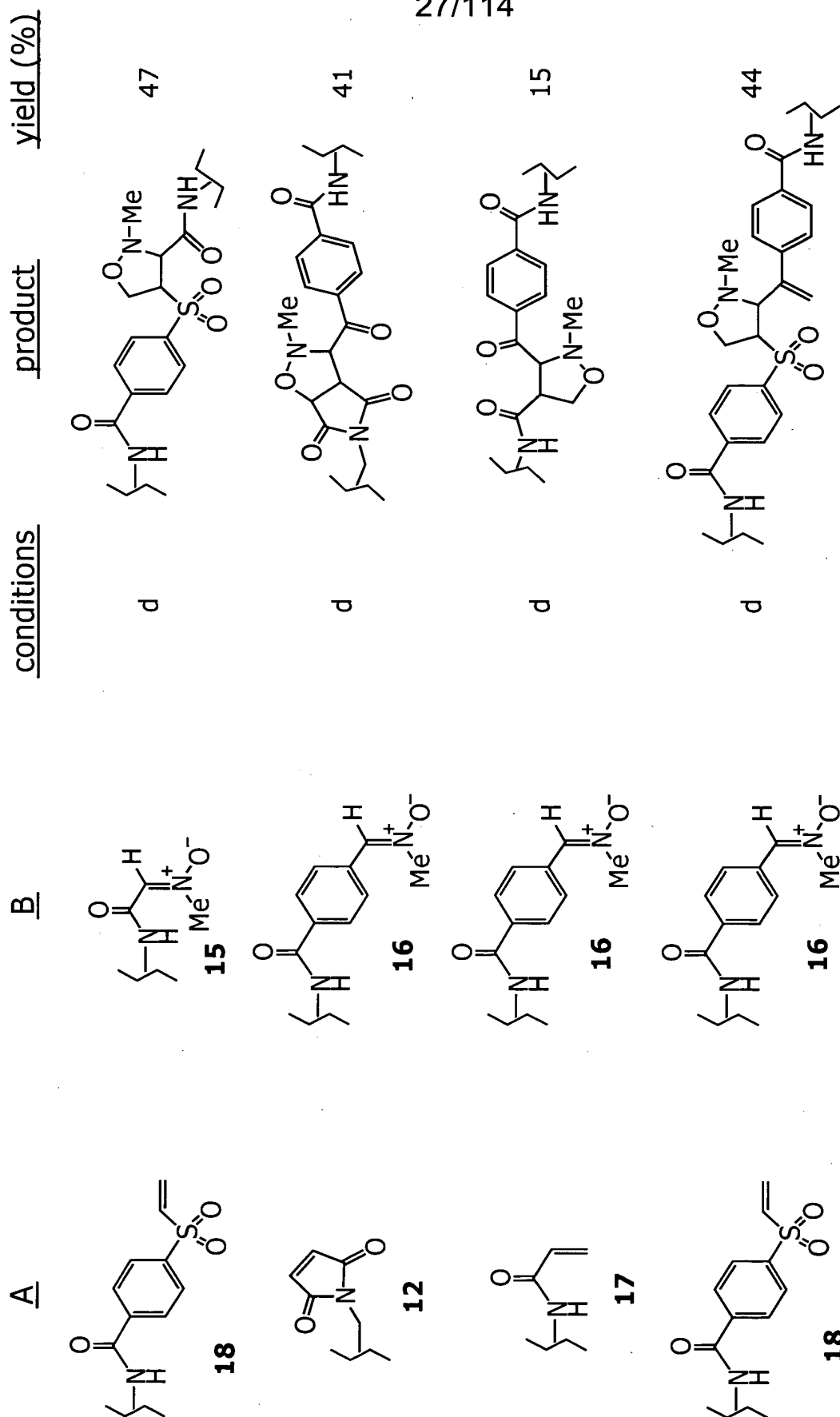


FIG. 23C

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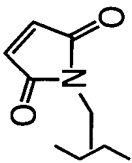
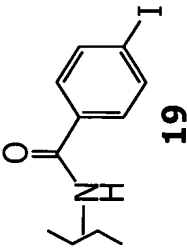
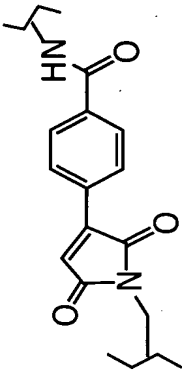
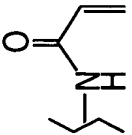
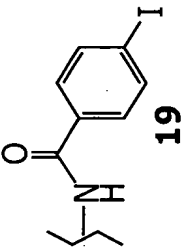
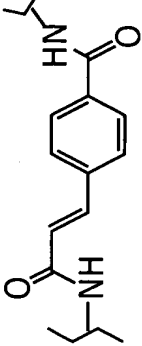
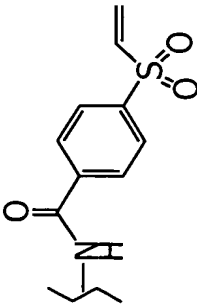
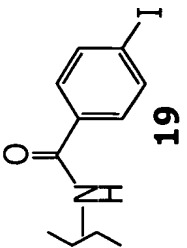
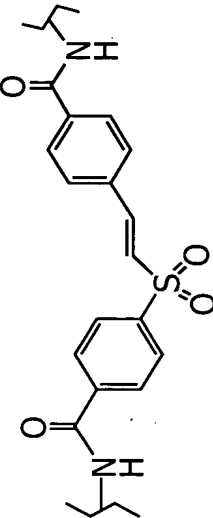
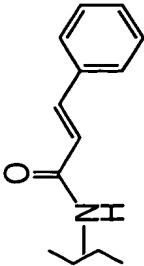
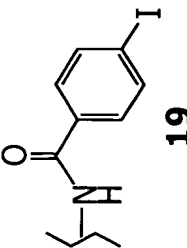
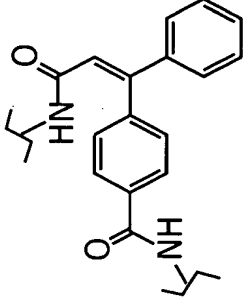
| <u>A</u>   | <u>B</u>   | <u>conditions</u> | <u>product</u>   | <u>yield (%)</u> |
|--|--|-------------------|--|------------------|
| <br><b>12</b>   | <br><b>19</b>   | e                 | <br><b>54</b>   |                  |
| <br><b>17</b>   | <br><b>19</b>   | f                 | <br><b>26</b>   |                  |
| <br><b>18</b>  | <br><b>19</b>  | f                 | <br><b>51</b>  |                  |
| <br><b>20</b> | <br><b>19</b> | f                 | <br><b>31</b> |                  |

FIG. 23D

| reaction:    | 1 + 3 | 4 + 6 | 10 + 11 | 11 + 13 | 12 + 15 | 18 + 19 |
|--------------|-------|-------|---------|---------|---------|---------|
| matchedness: | M     | M     | M       | M       | M       | M       |
|              | X     | X     | X       | X       | X       | X       |

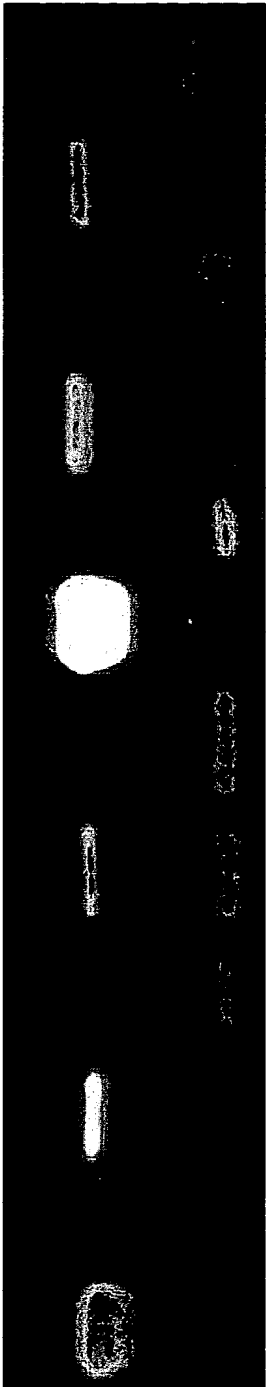


FIG. 24

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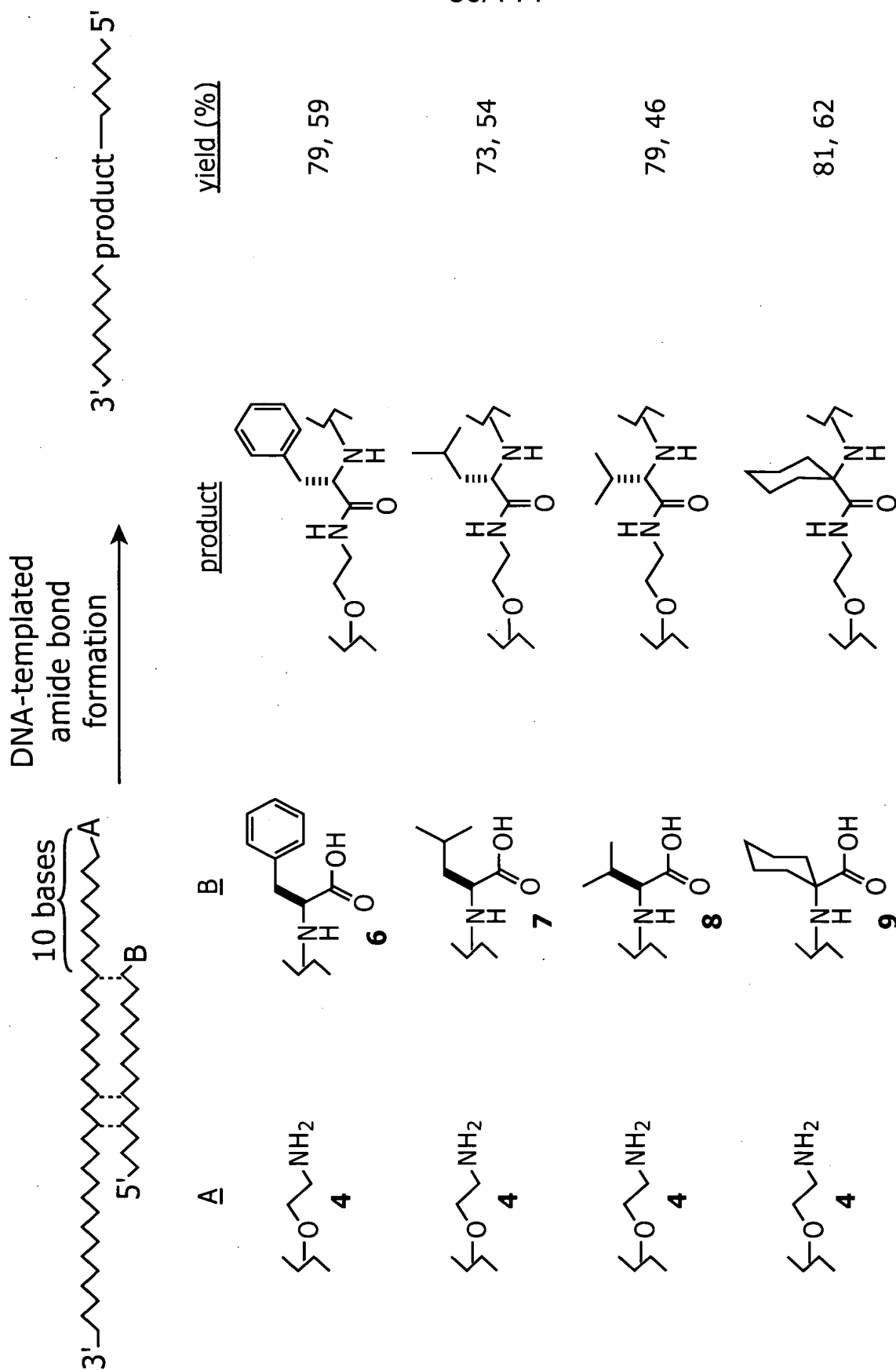


FIG. 25A

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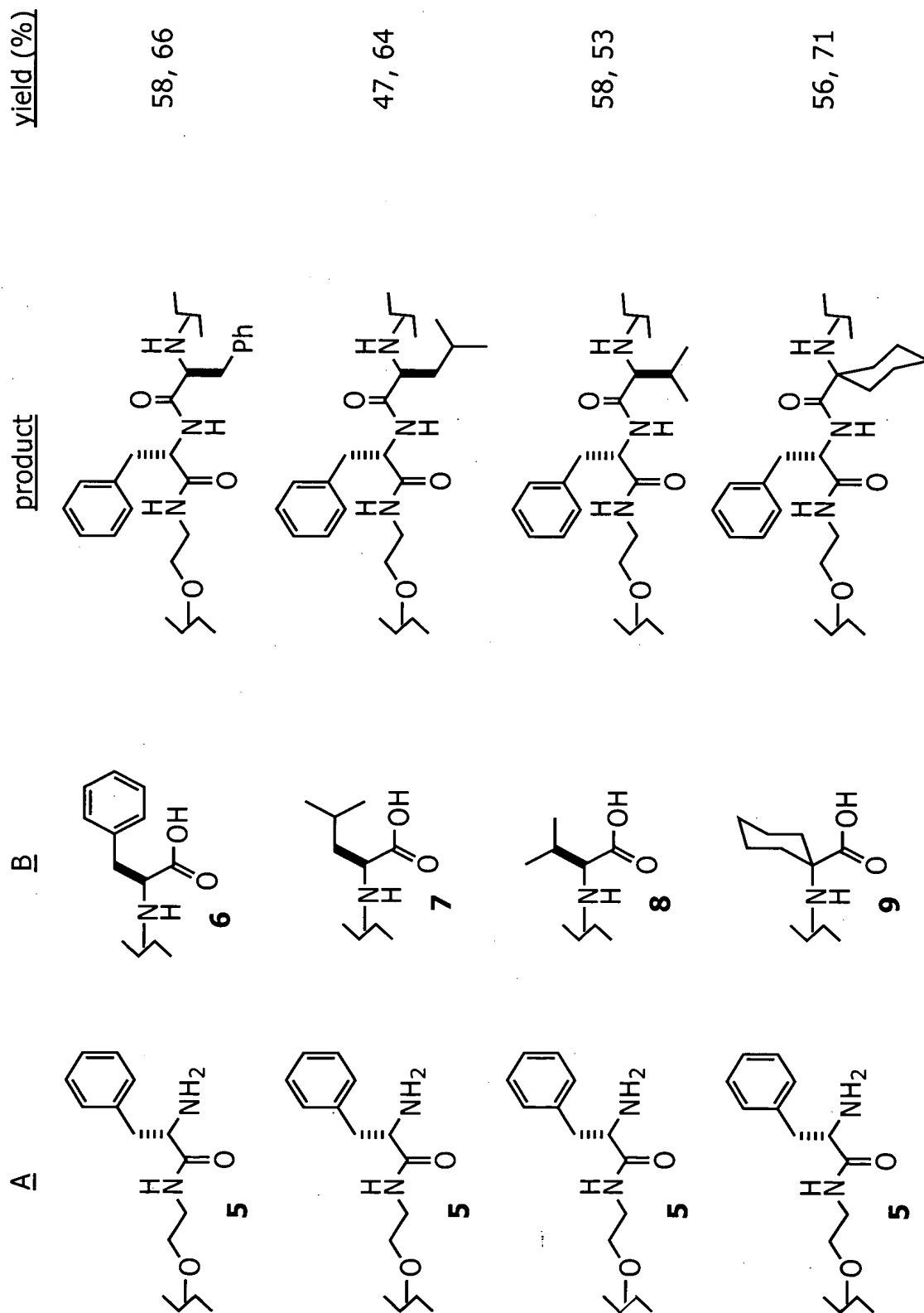


FIG. 25B

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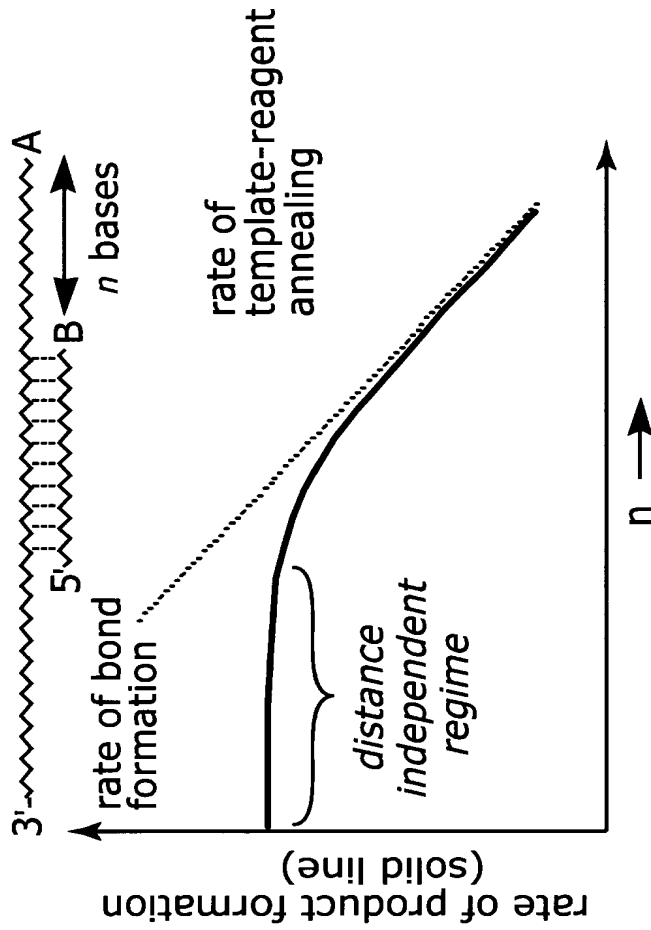


FIG. 26A

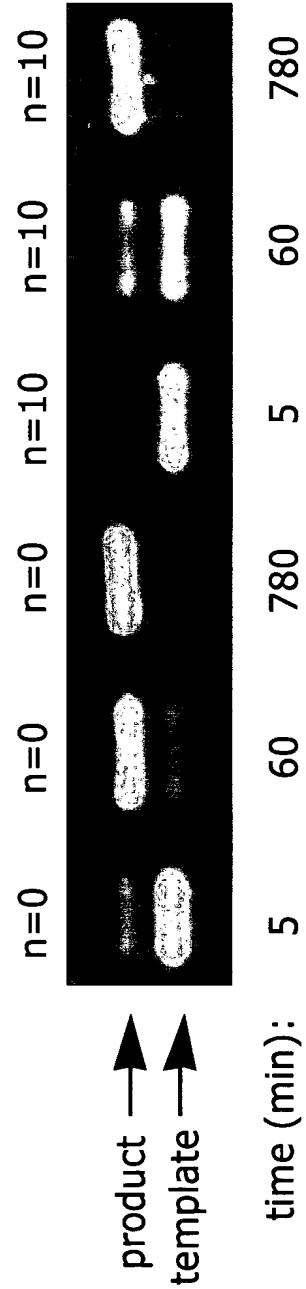


FIG. 26B



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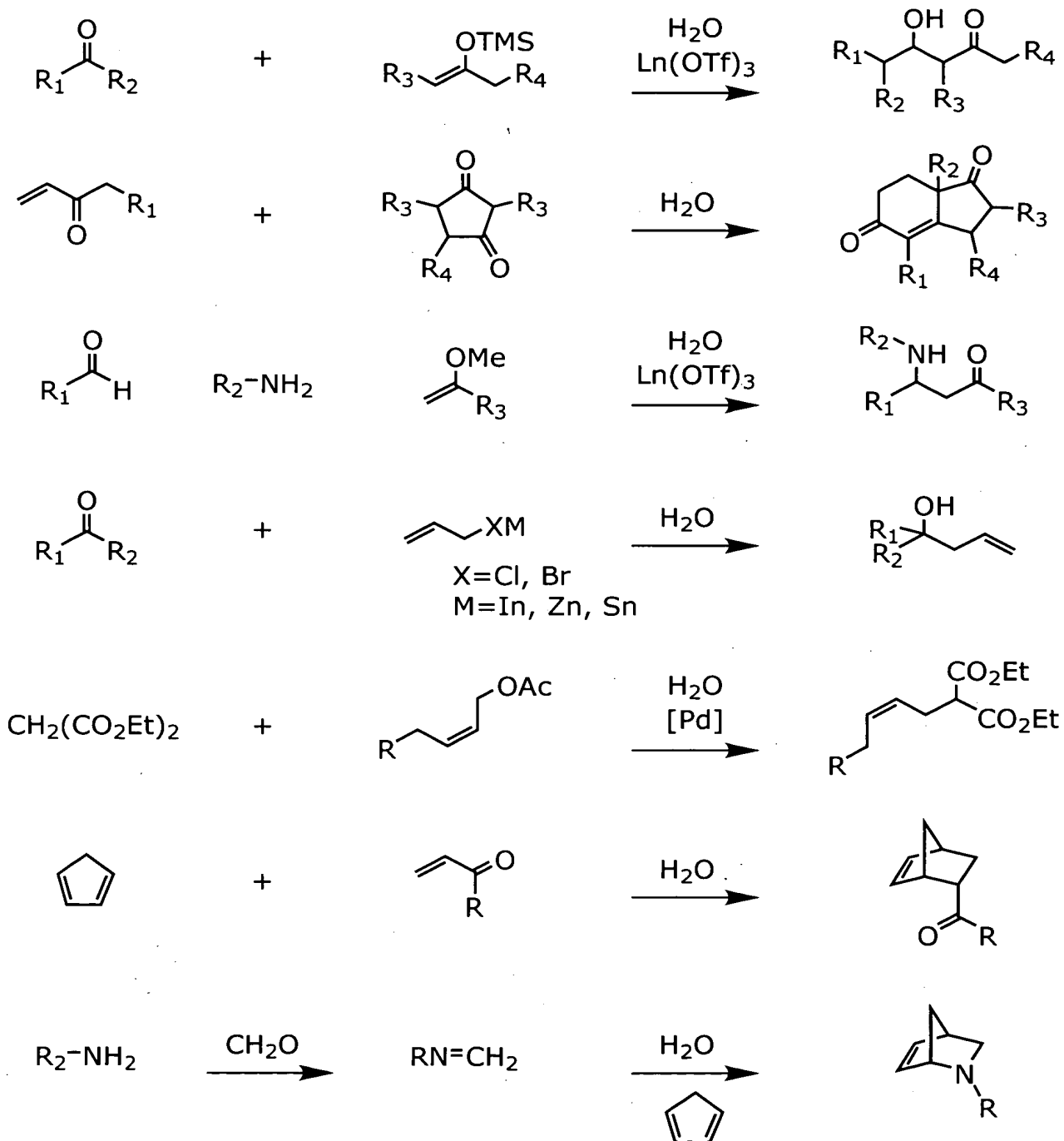


FIG. 27

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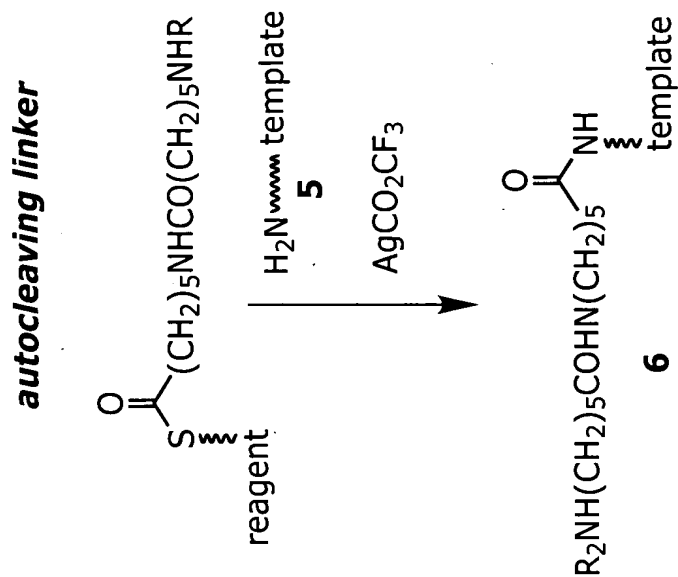


FIG. 28B

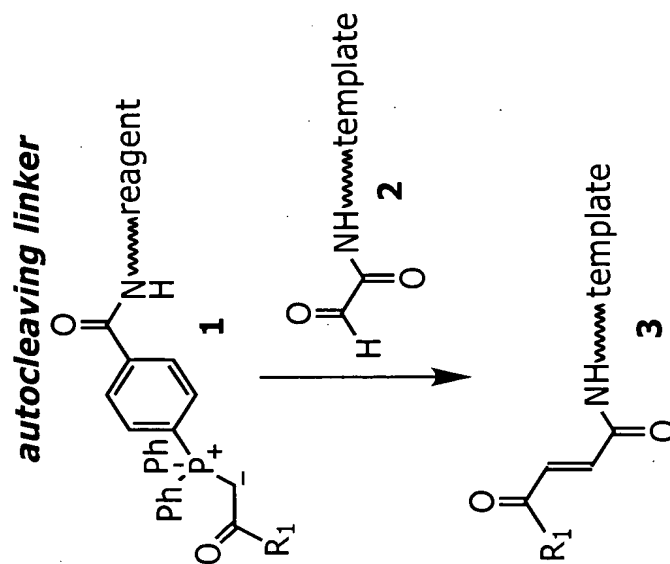


FIG. 28A

**useful scar linker**

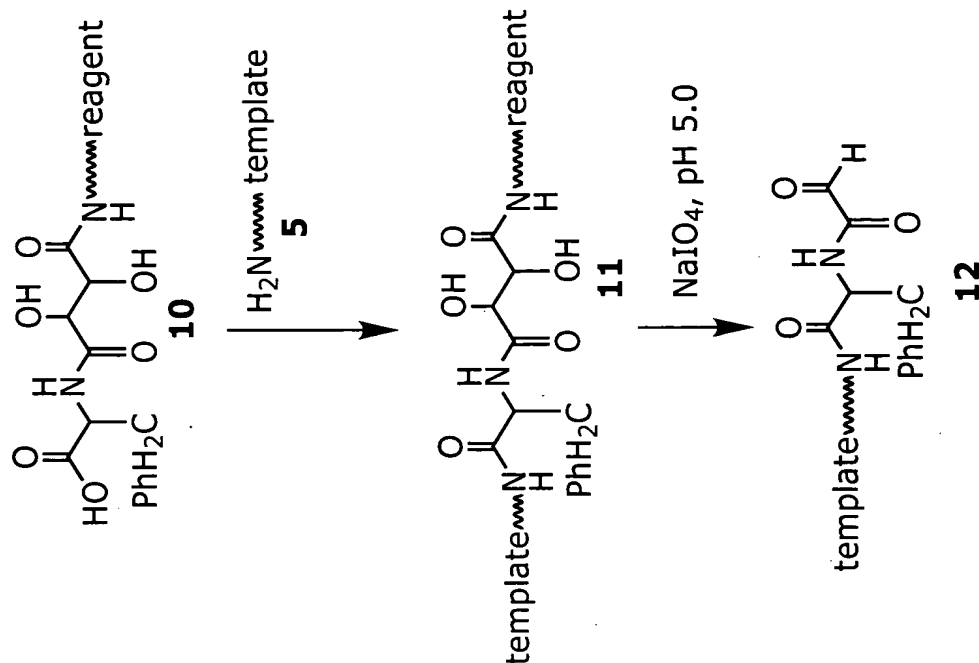
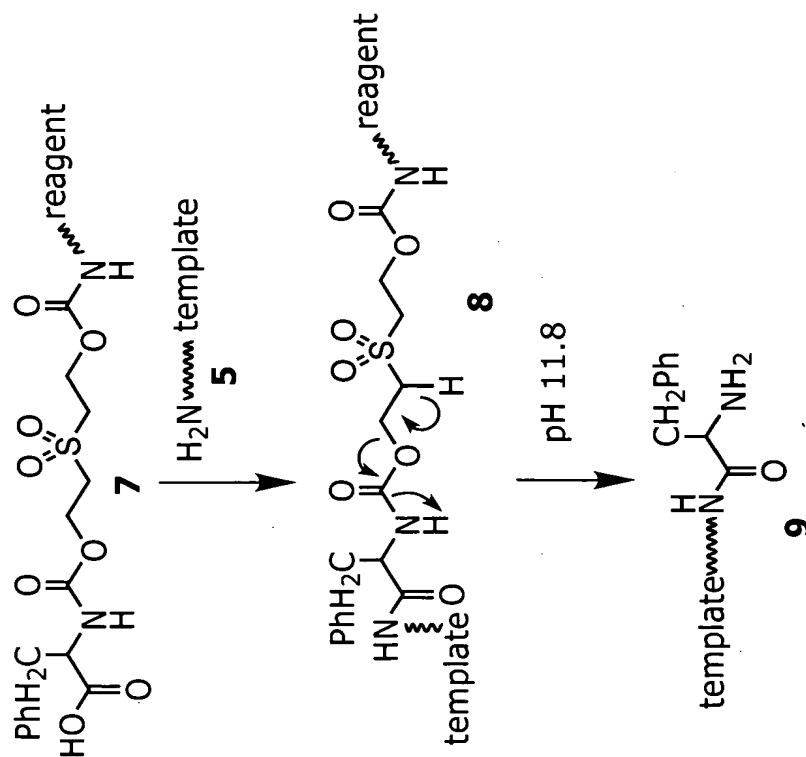


FIG. 28D

**scarless linker**



**FIG. 28C**

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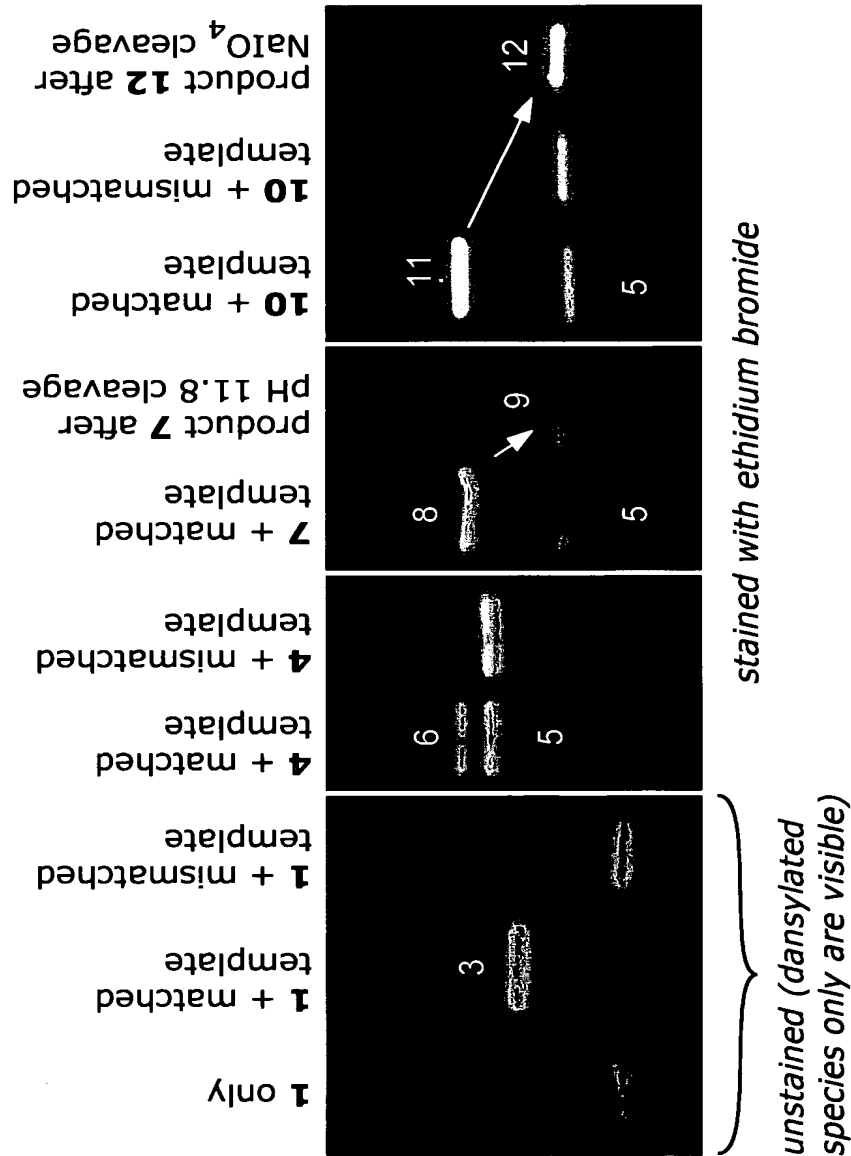


FIG. 29

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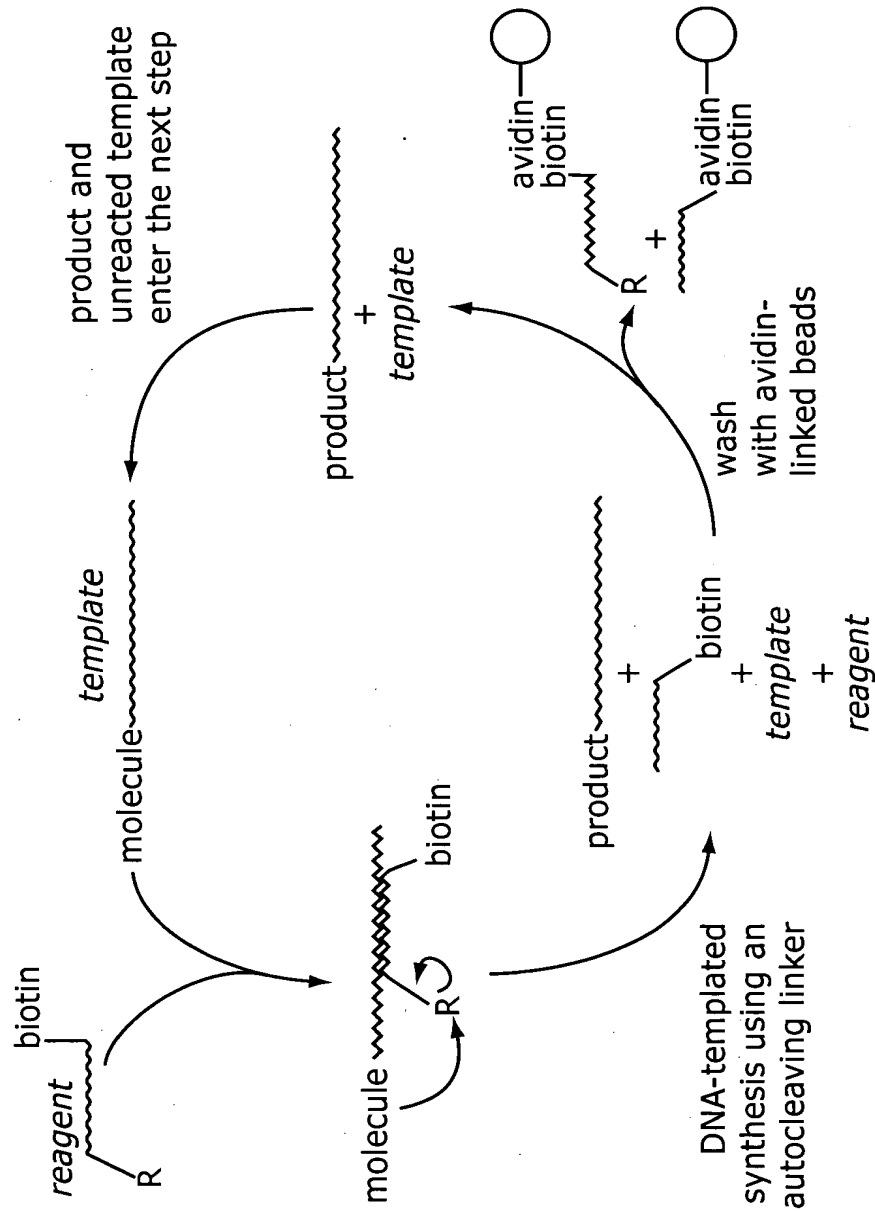


FIG. 30A

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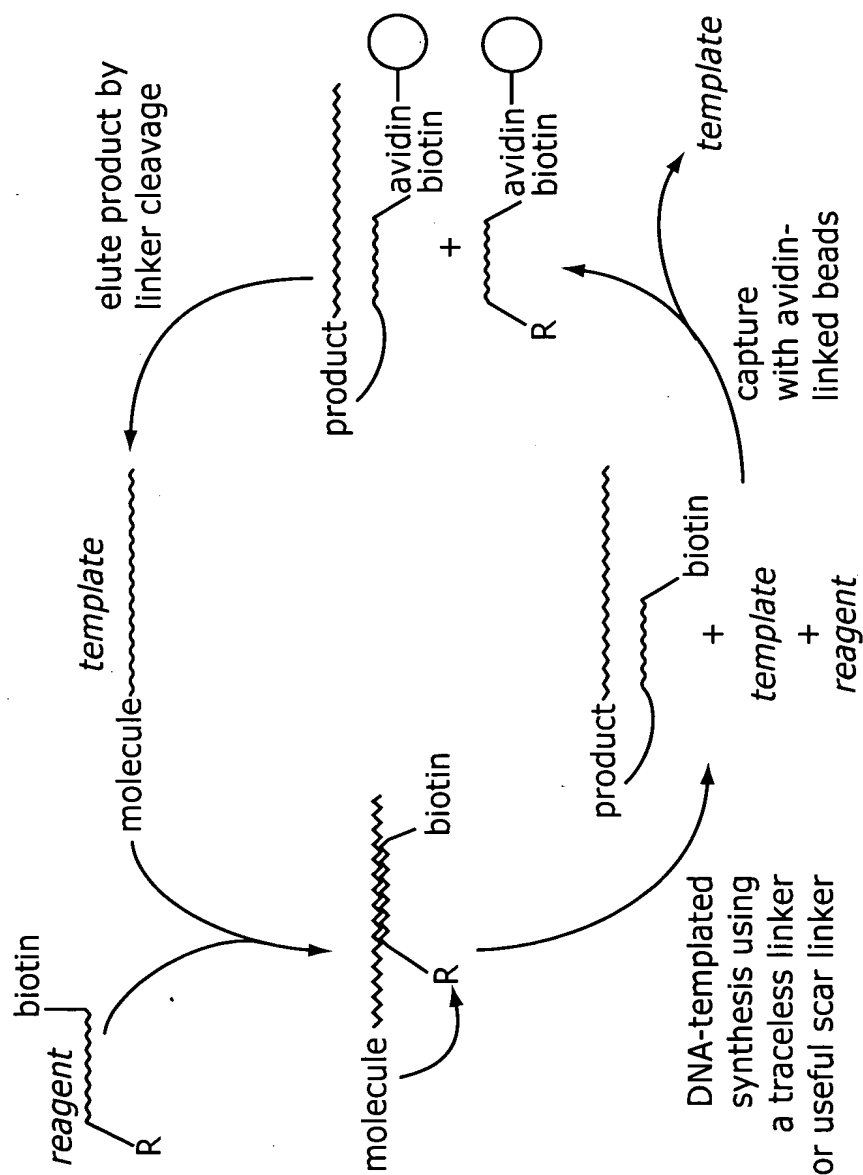


FIG. 30B

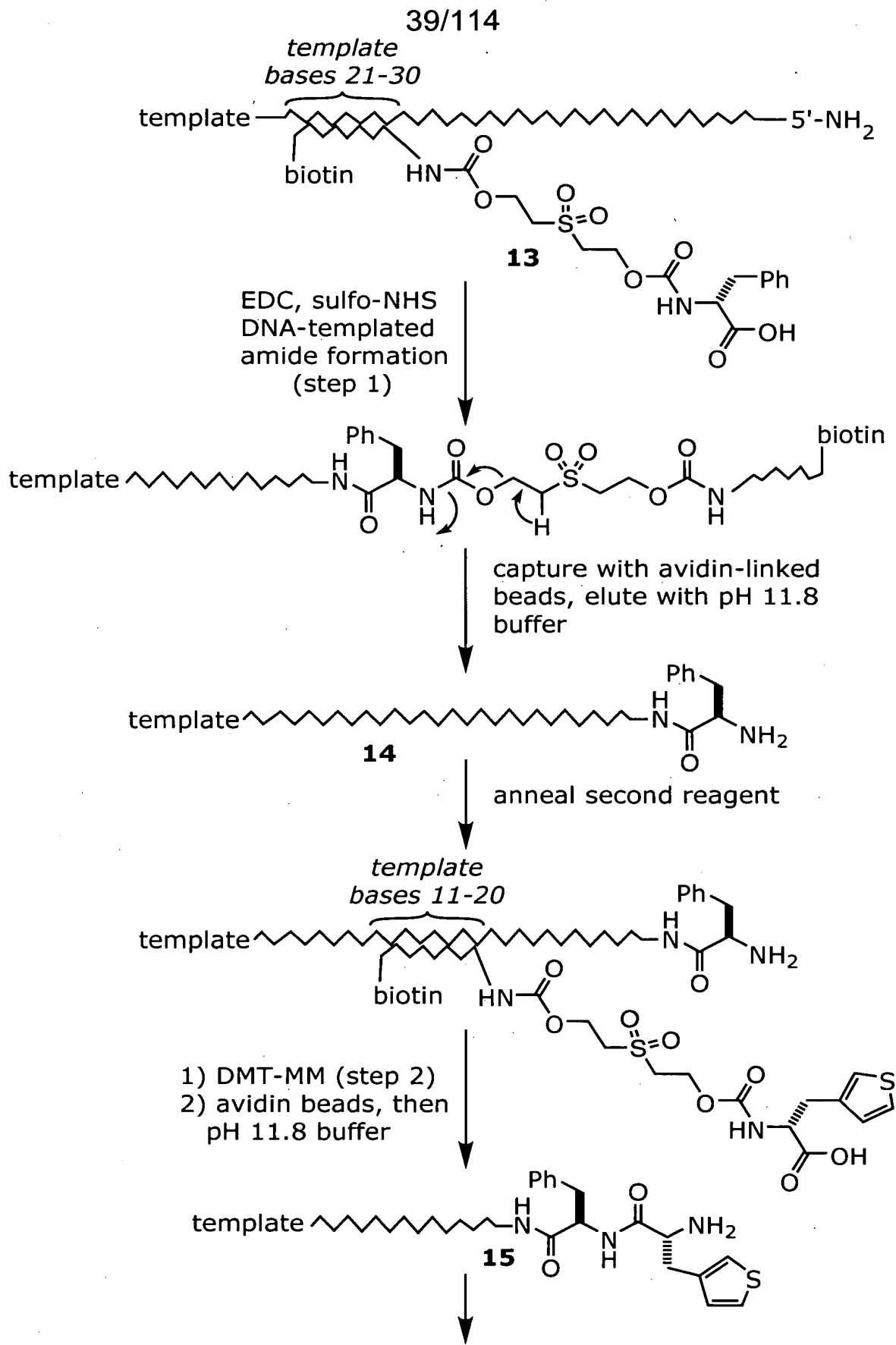


FIG. 31A

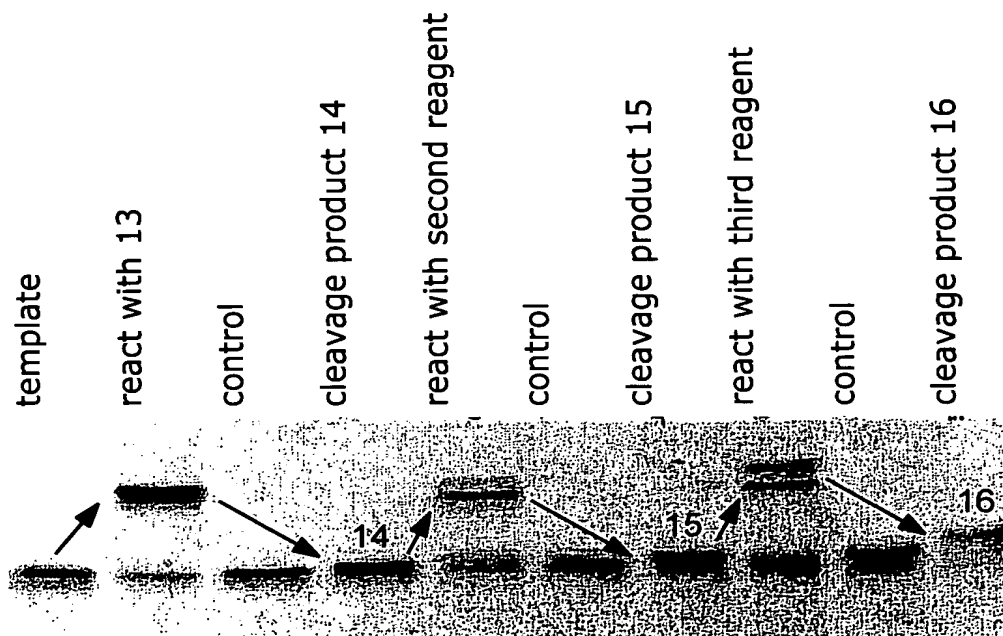
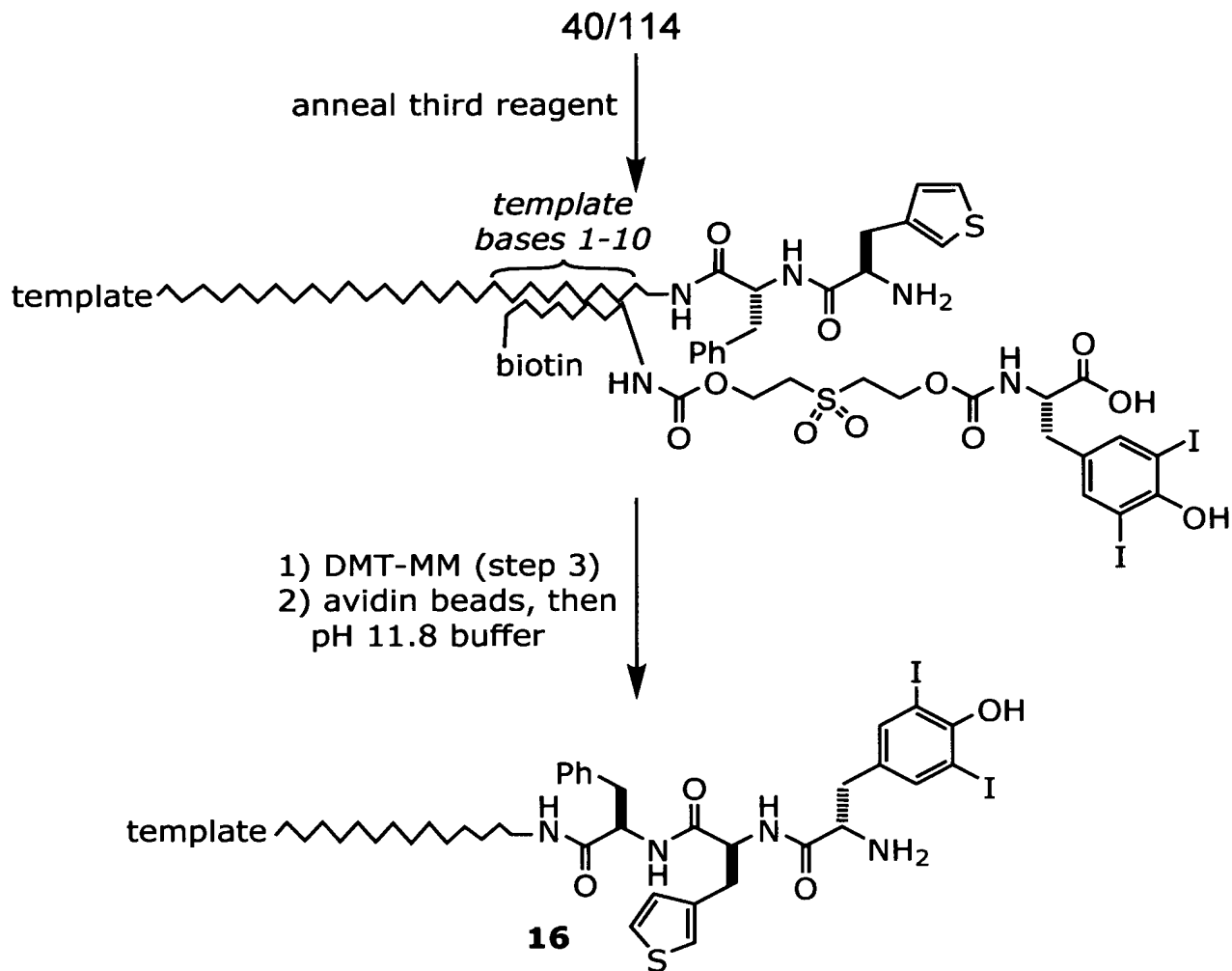


FIG. 31B



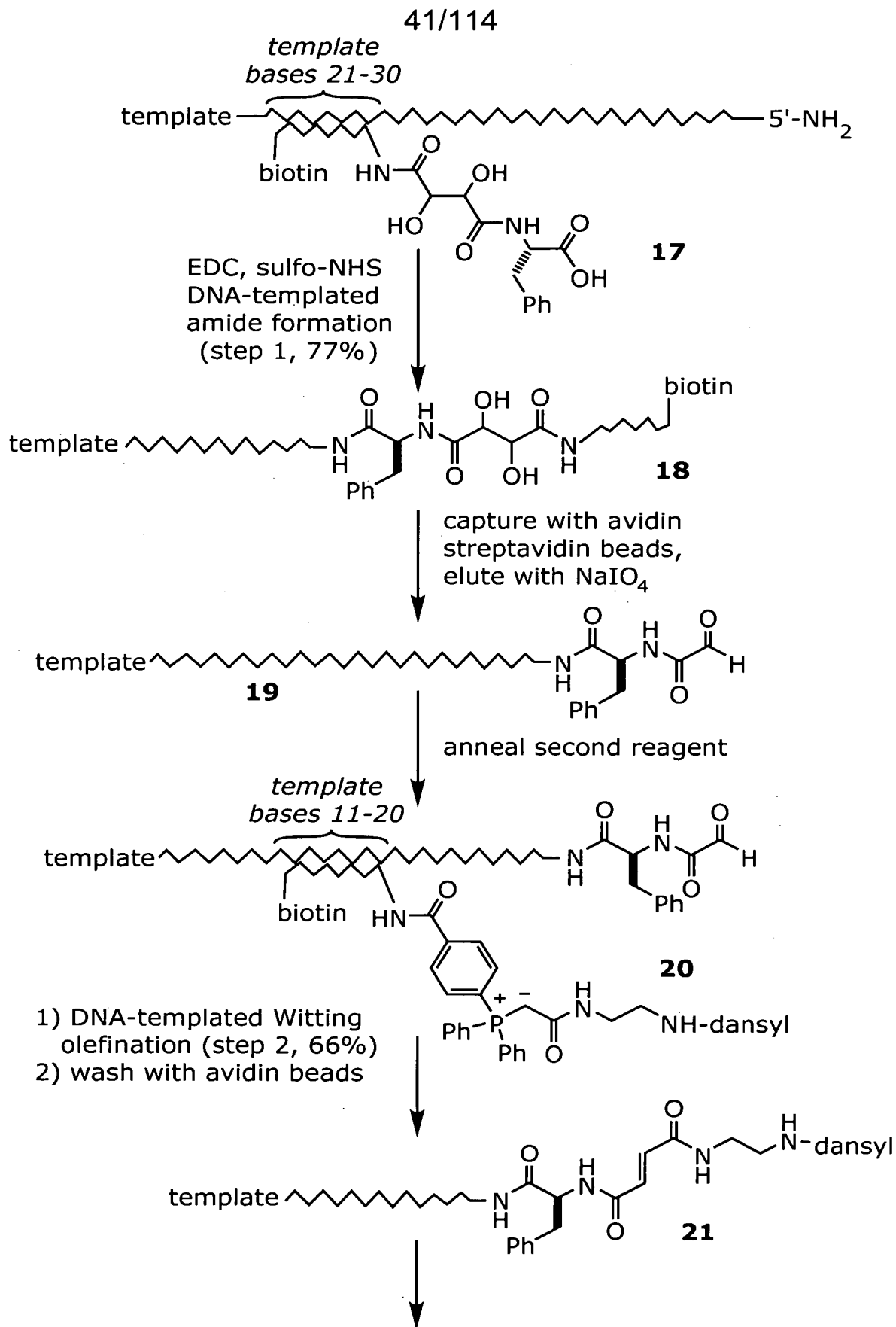


FIG. 32A

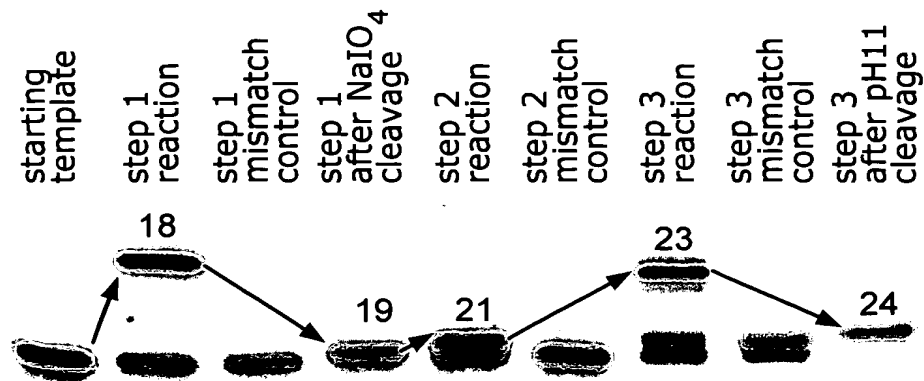
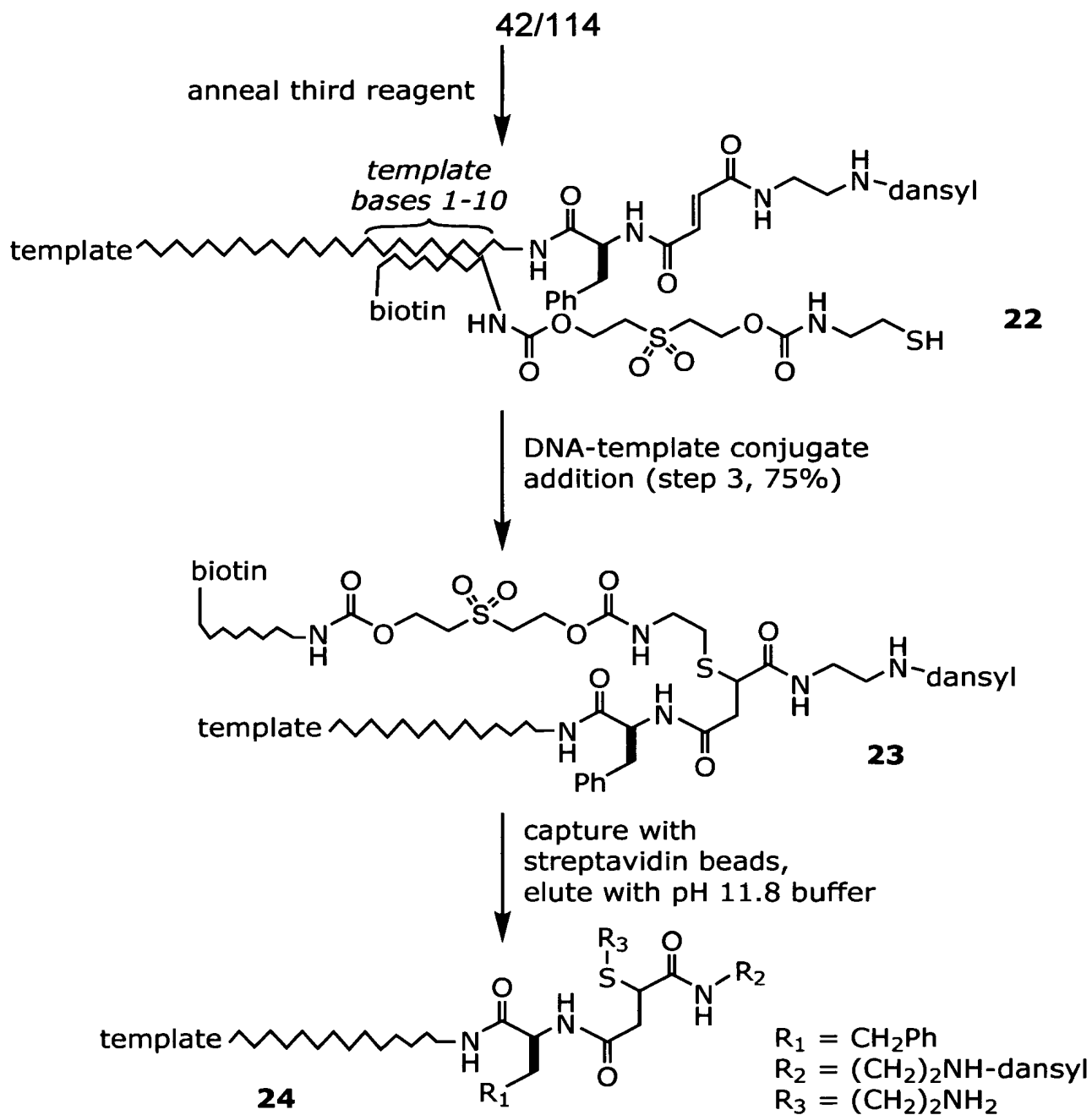
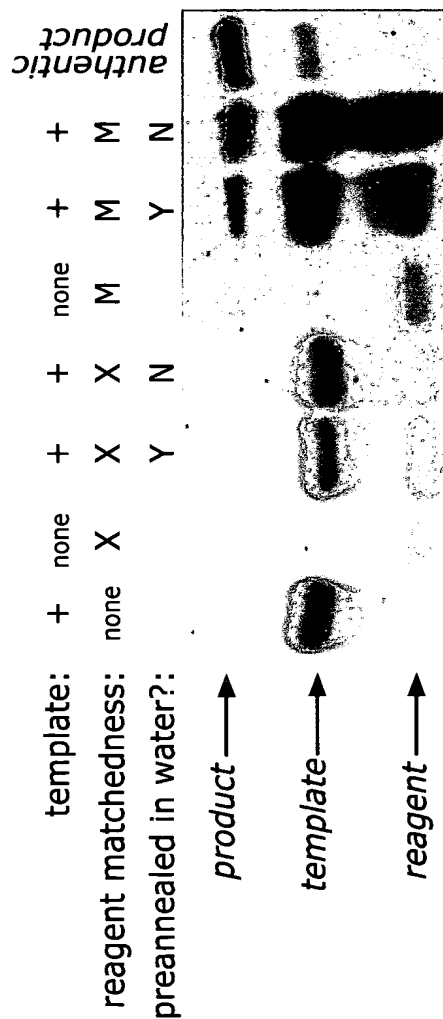


FIG. 32B



**FIG. 33**

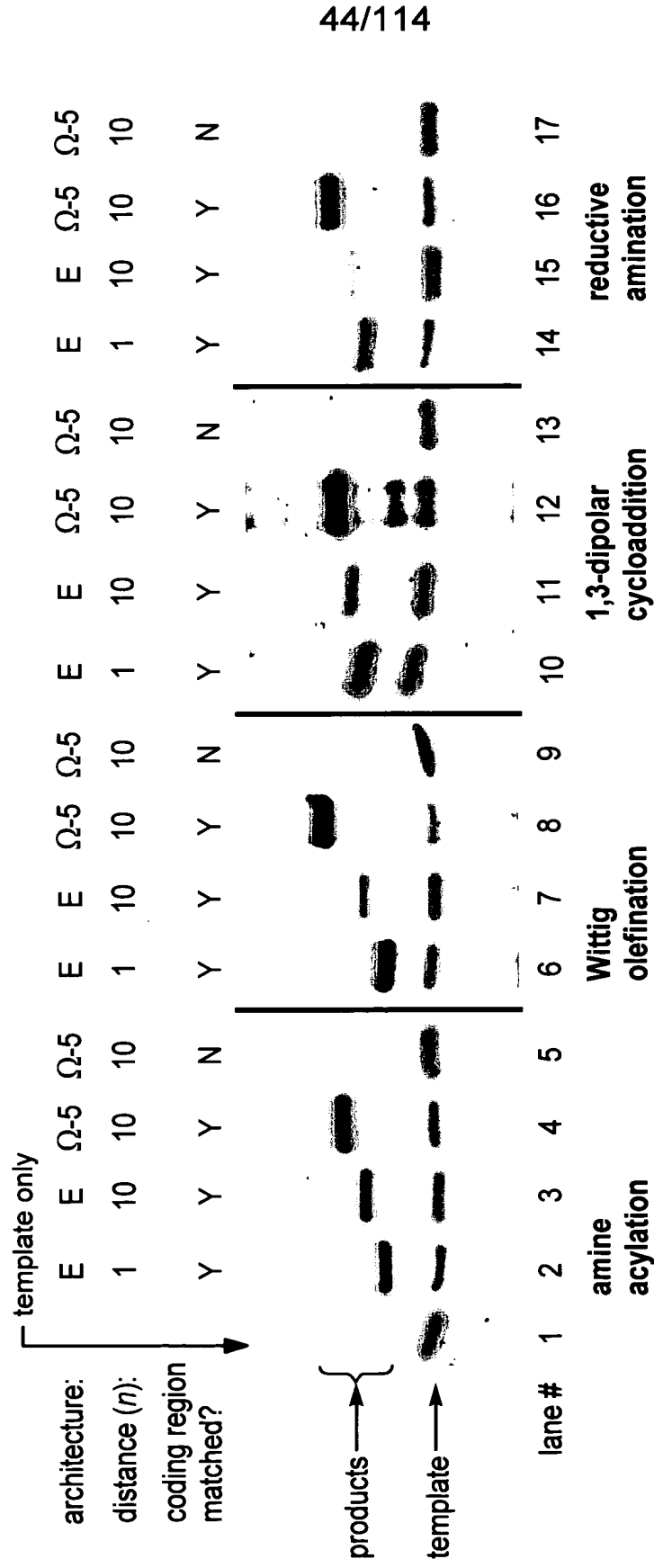
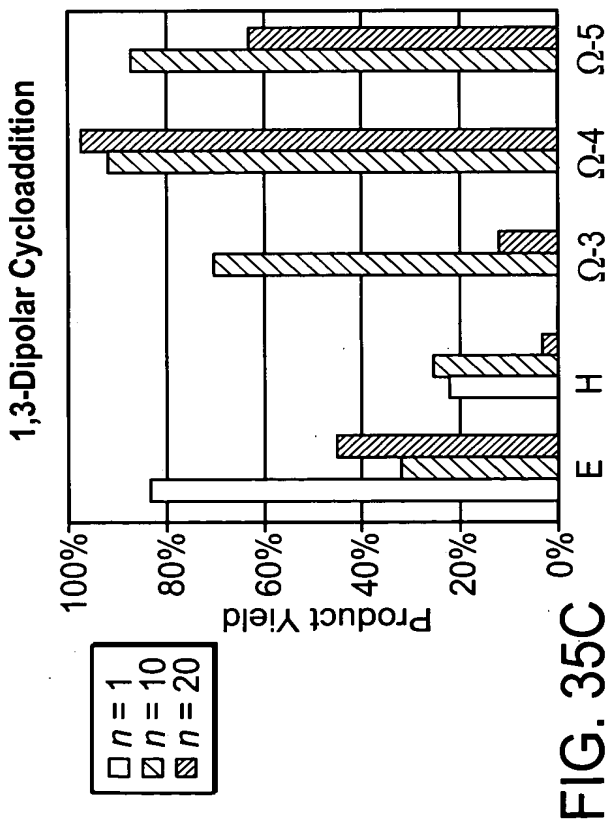
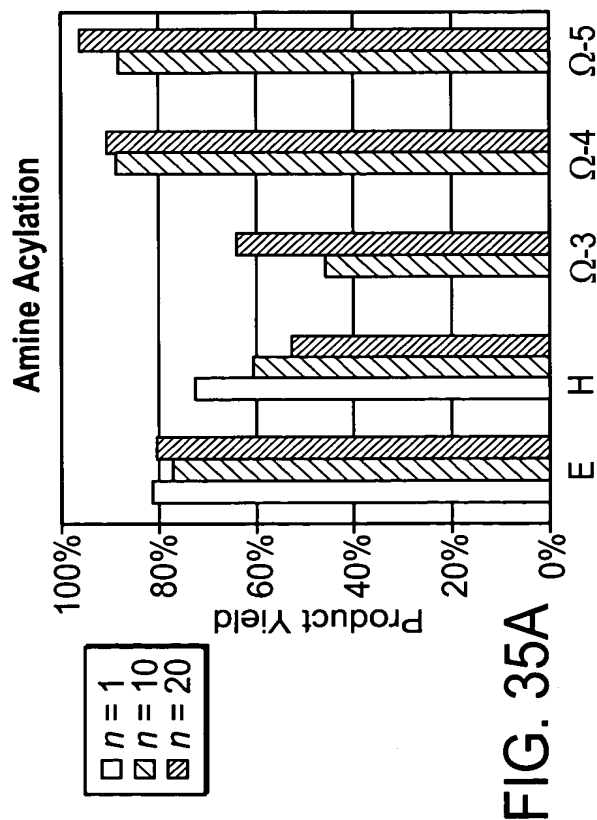
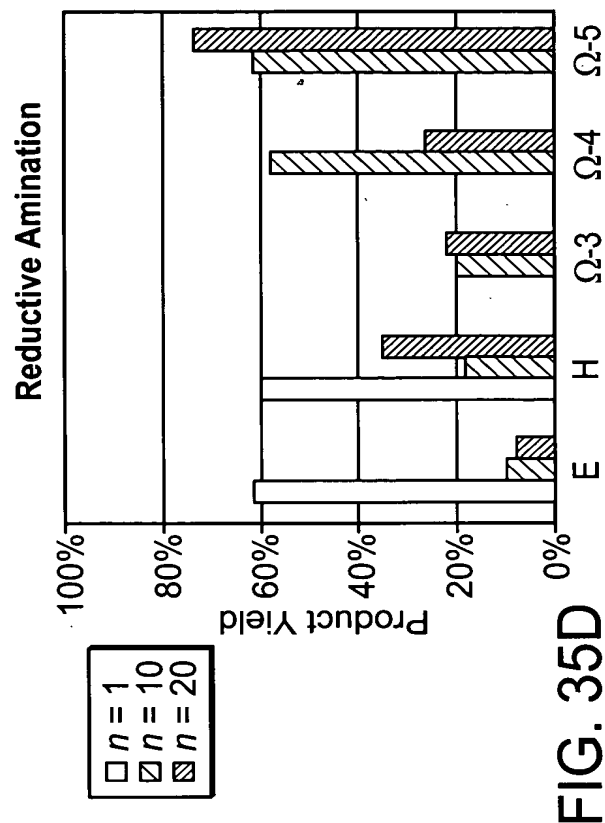
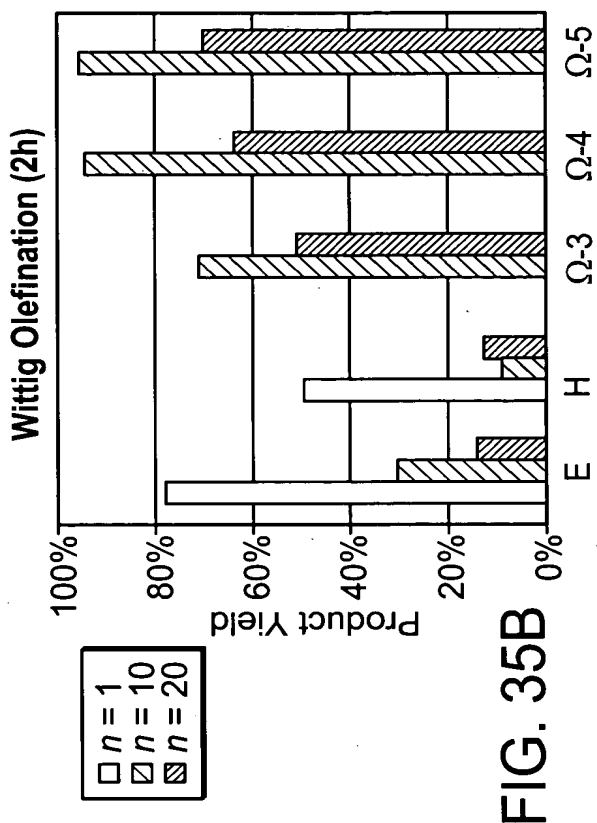


FIG. 34

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| <u>Architecture</u>   | <u>Buffer</u> | <u><math>T_m</math> (°C)</u> |
|-----------------------|---------------|------------------------------|
| E ( $n = 10$ )        | PBS           | 45                           |
| $\Omega$ ( $n = 10$ ) | PBS           | 46                           |
| E ( $n = 10$ )        | HSP           | 55                           |
| $\Omega$ ( $n = 10$ ) | HSP           | 54                           |
| E ( $n = 20$ )        | PBS           | 40                           |
| $\Omega$ ( $n = 20$ ) | PBS           | 39                           |

FIG. 36

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|  |   |
|--|---|
|  $n = -1$ |  $n = 3$ |
|  $n = 1$  |  $n = 4$ |
|  $n = 2$  |  $n = 5$ |

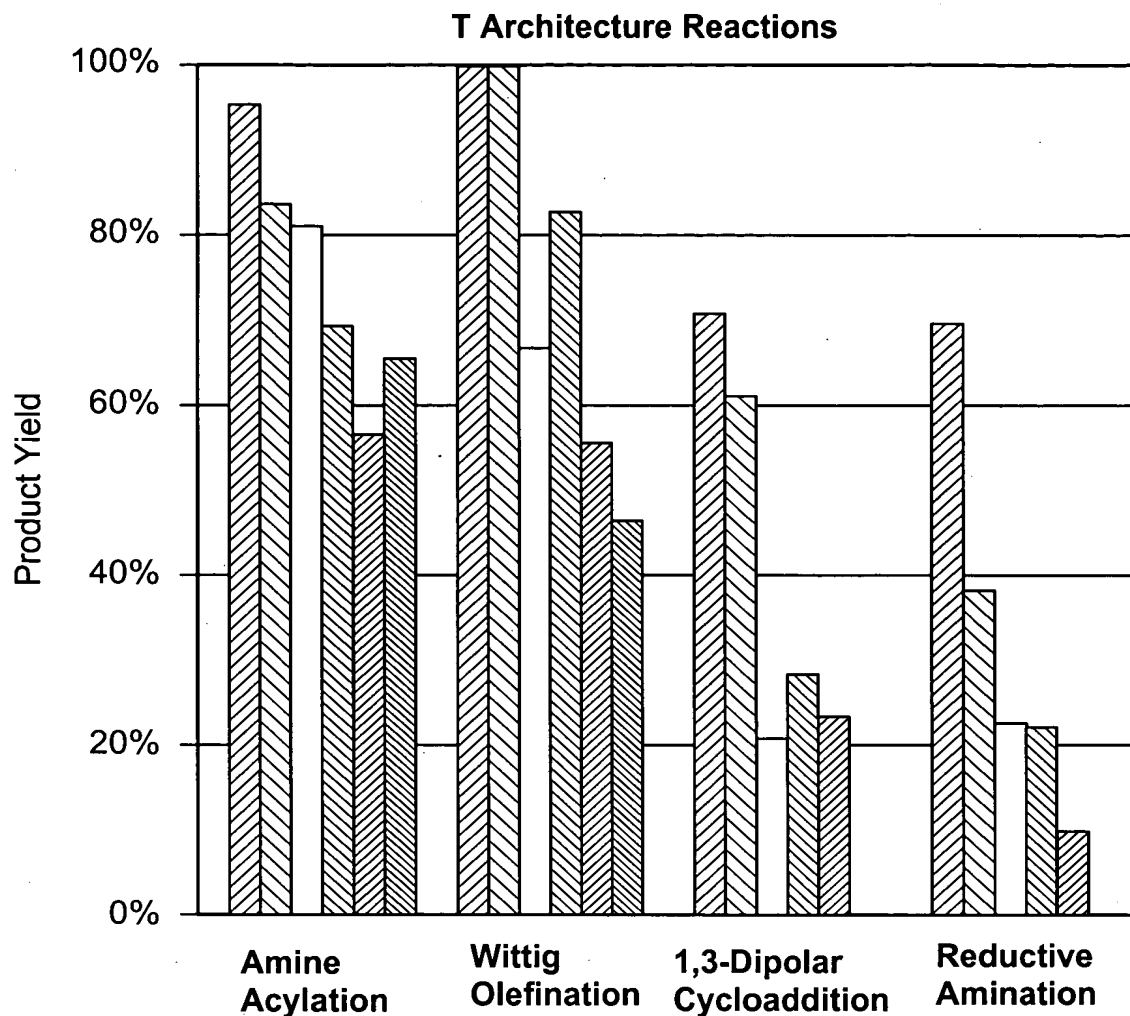


FIG. 37

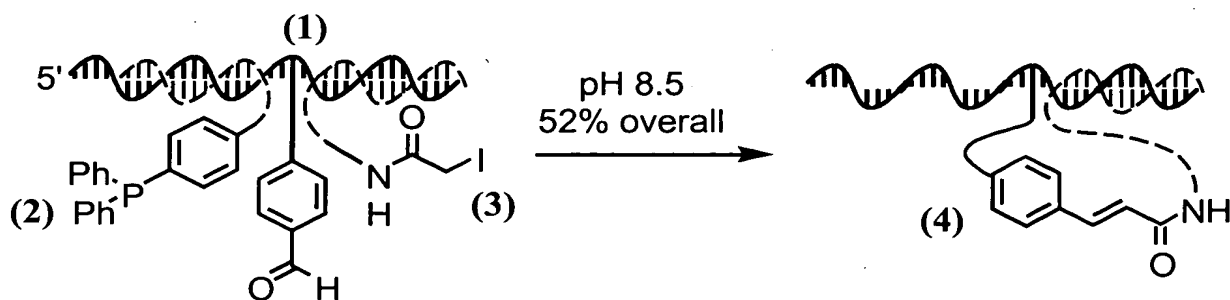


FIG. 38A

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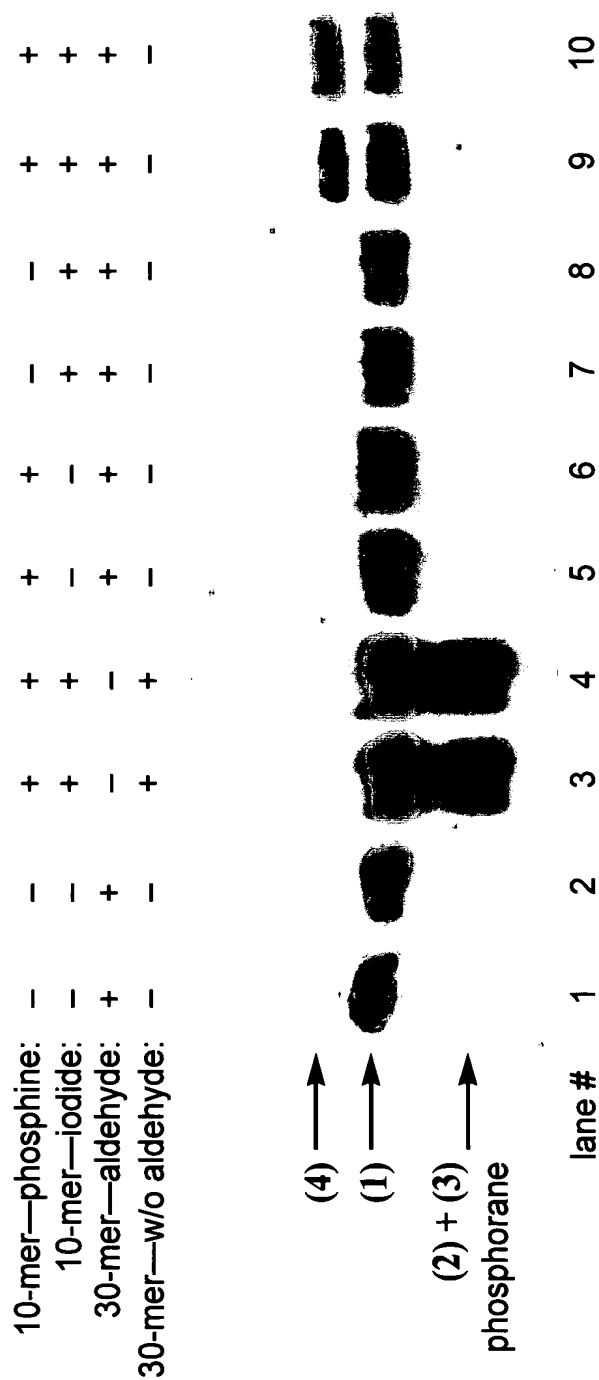


FIG. 38B

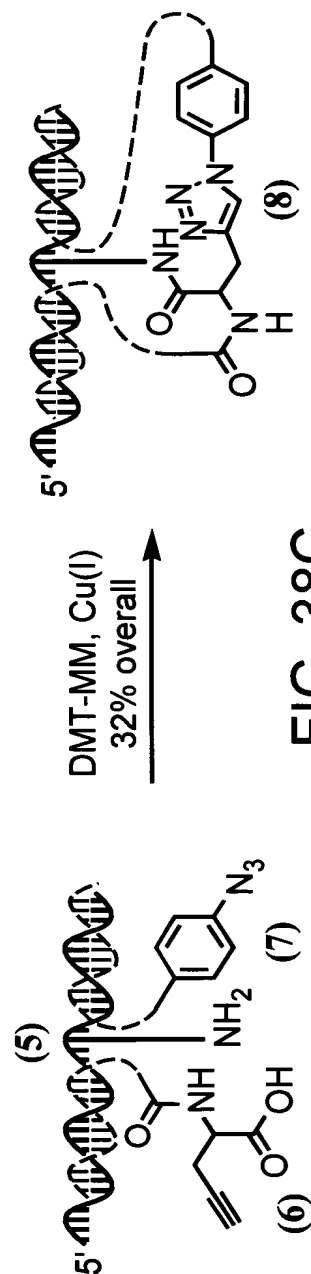


FIG. 38C



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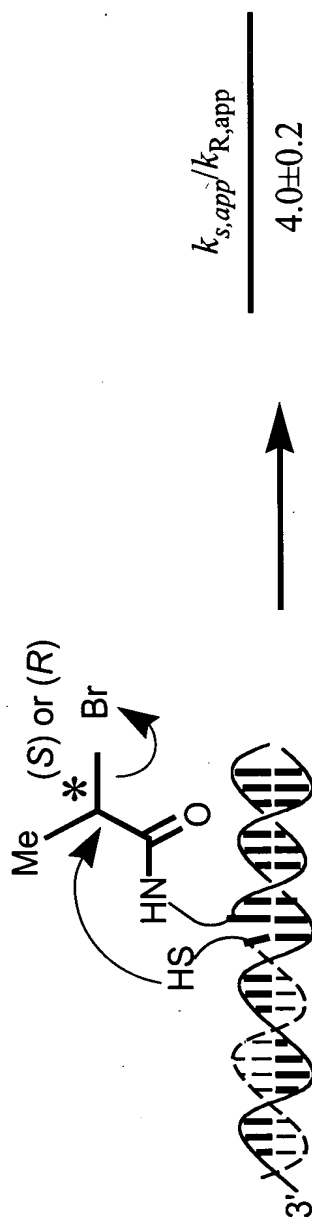


FIG. 39A

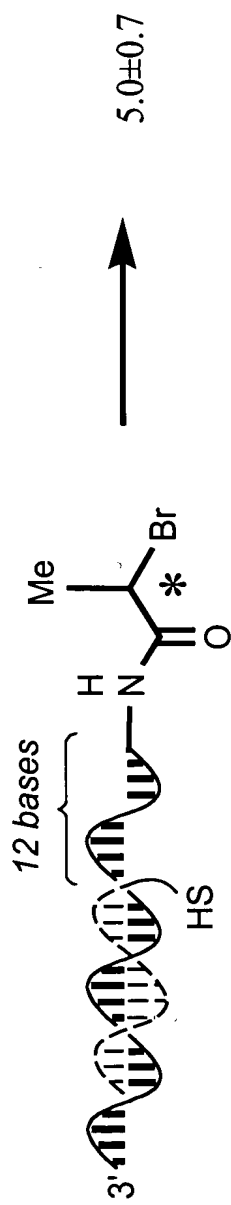


FIG. 39B

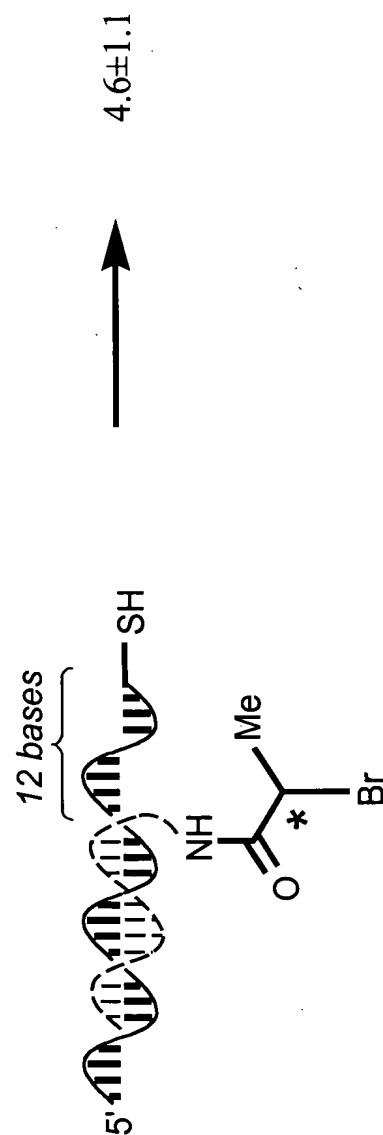


FIG. 39C

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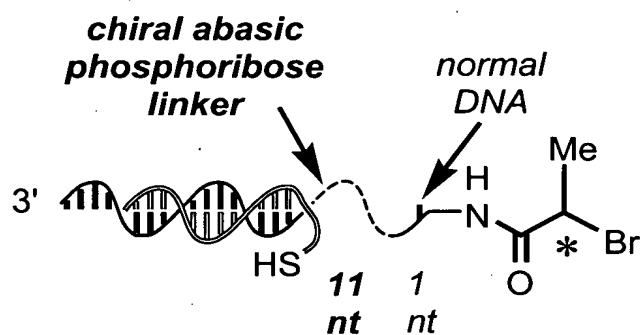


FIG. 40A

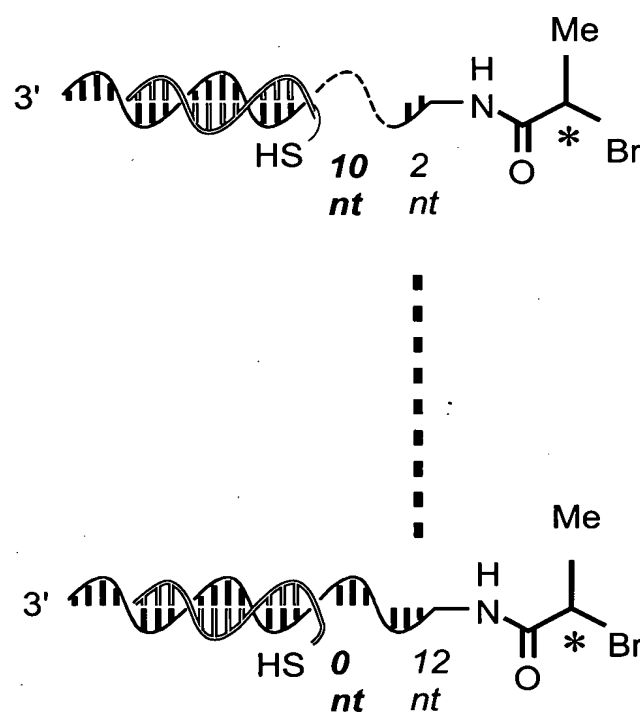


FIG. 40B

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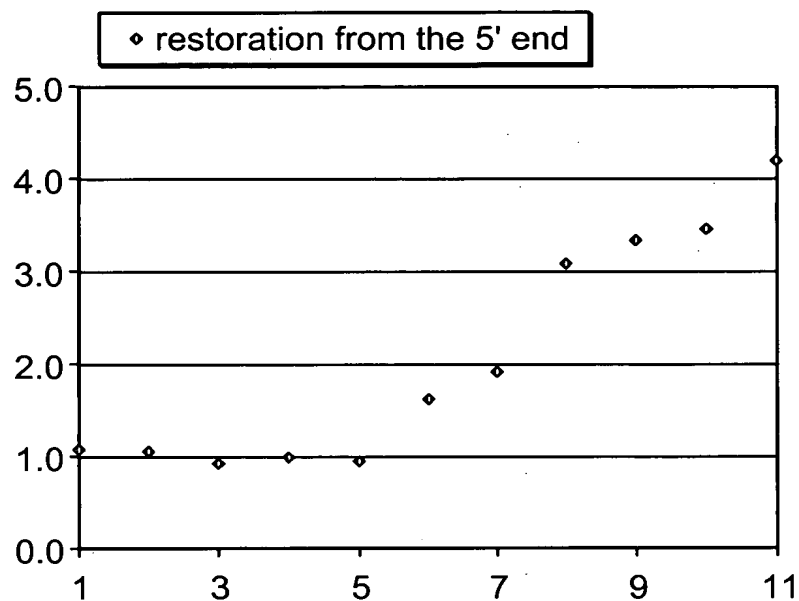


FIG. 40C

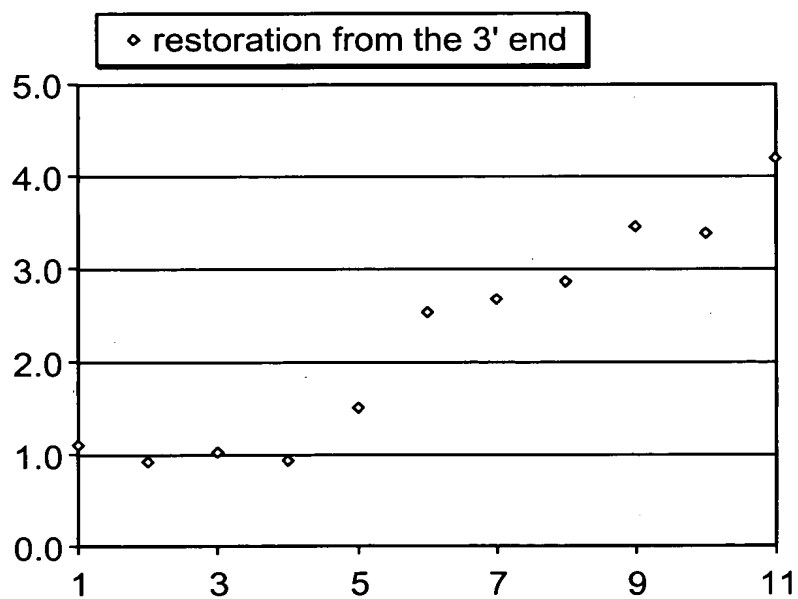


FIG. 40D

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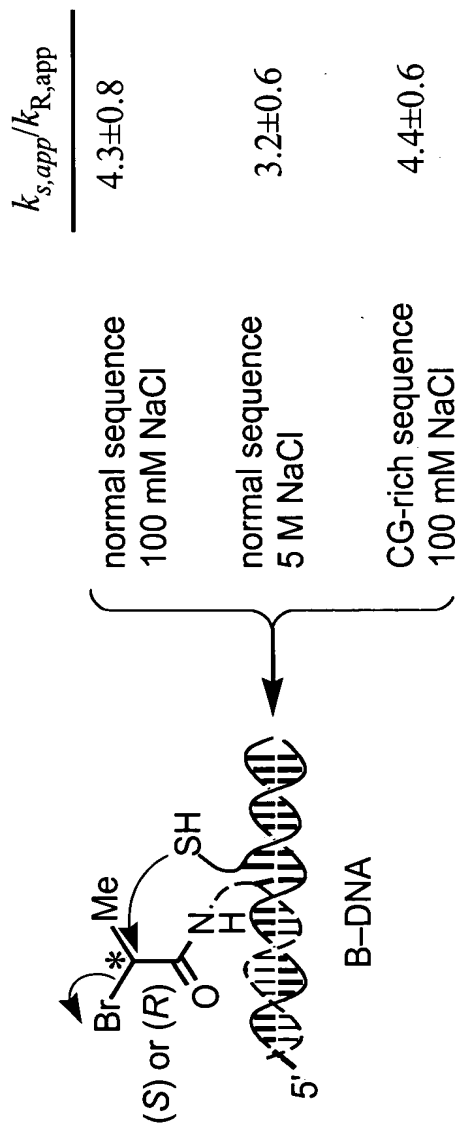


FIG. 41A

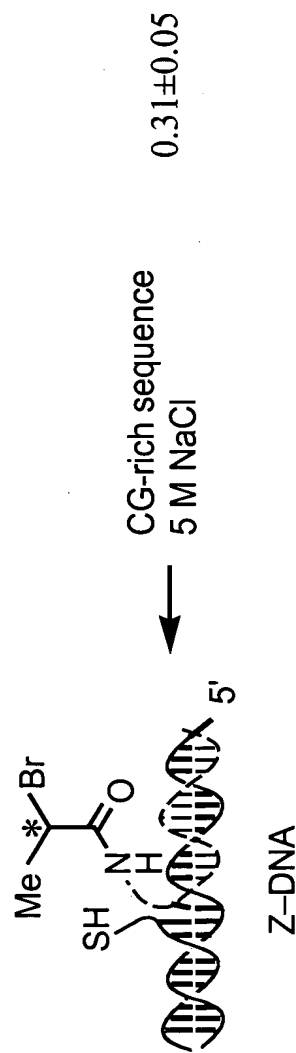


FIG. 41B

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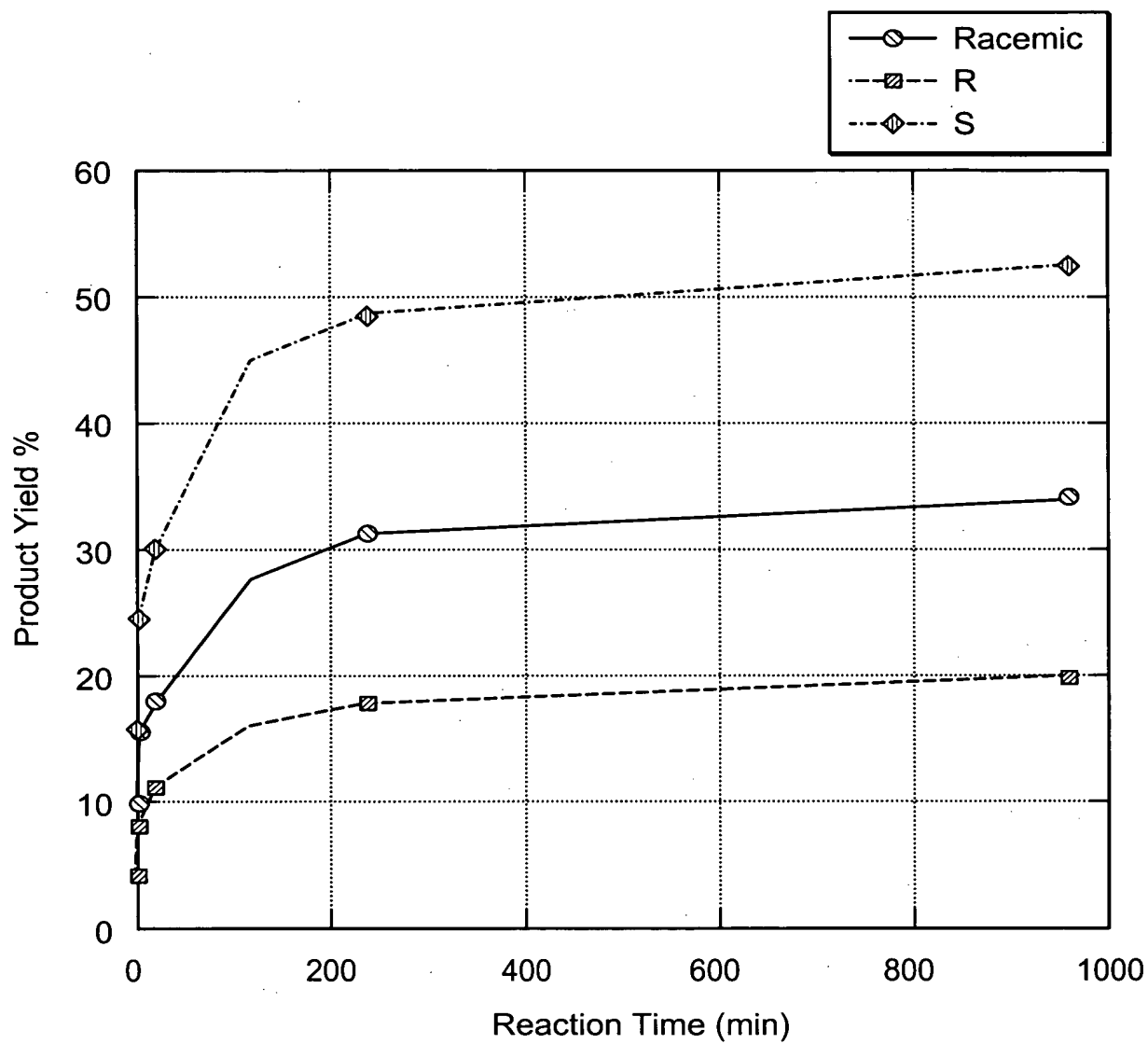


FIG. 42A

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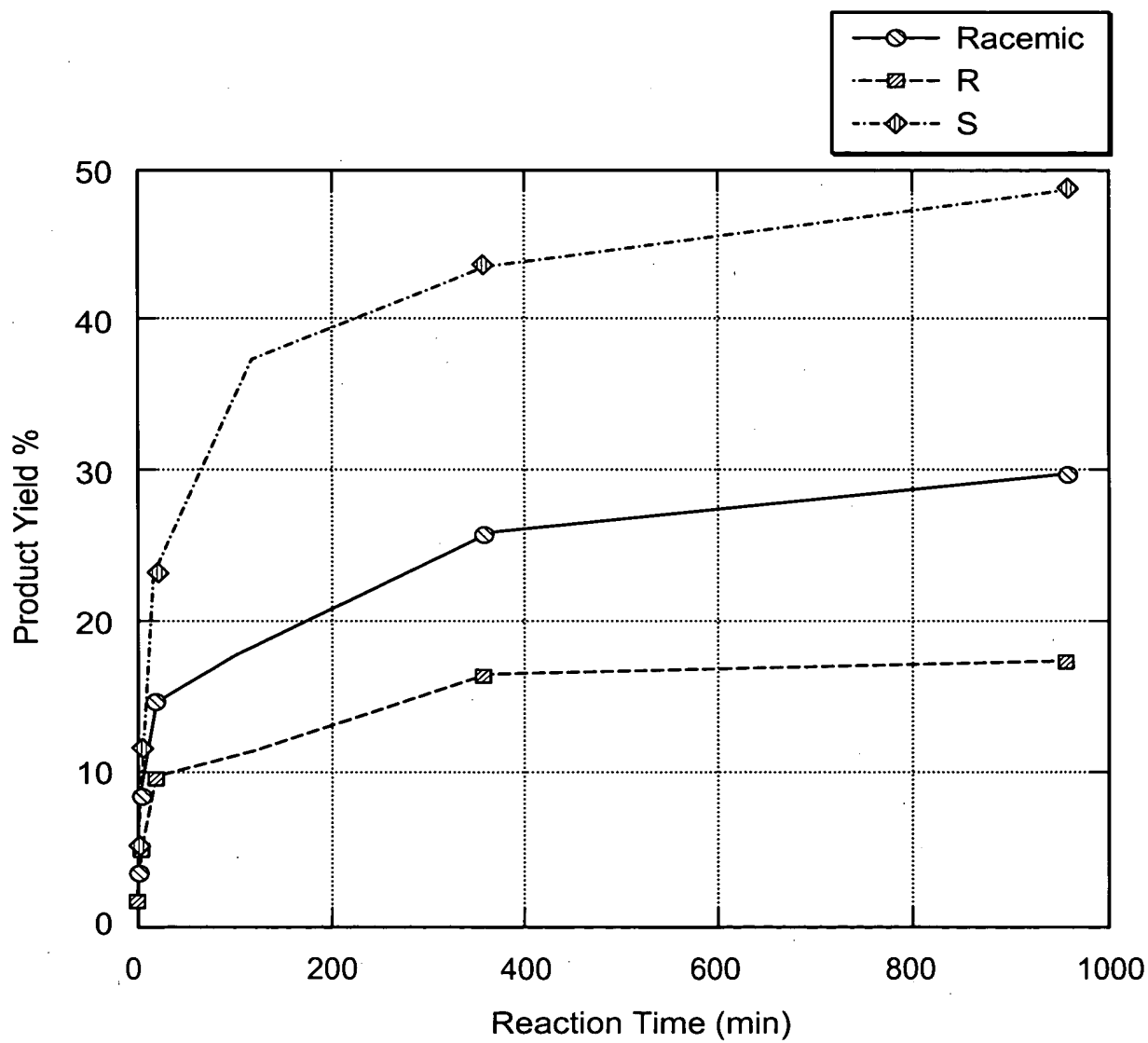


FIG. 42B

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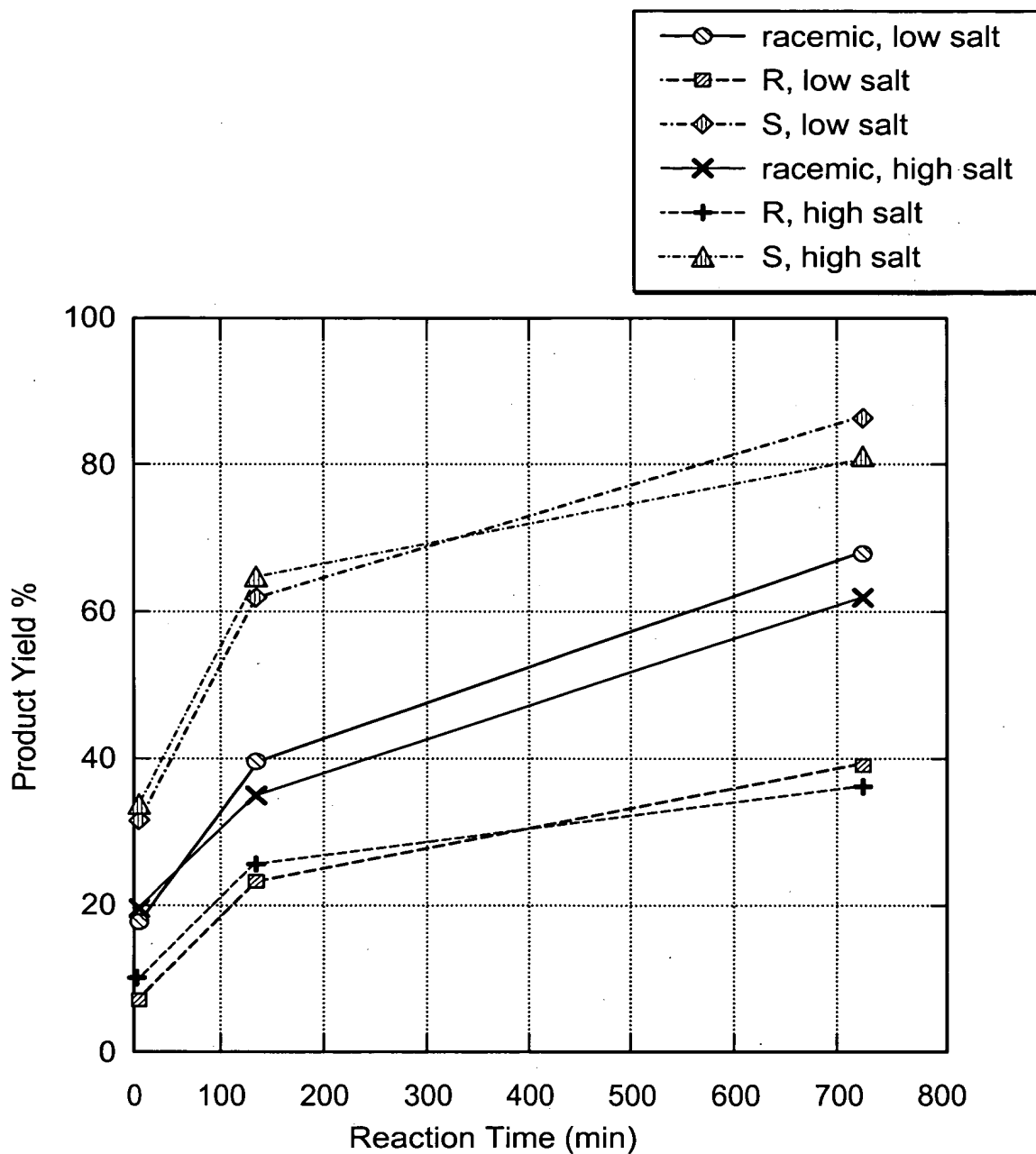


FIG. 42C

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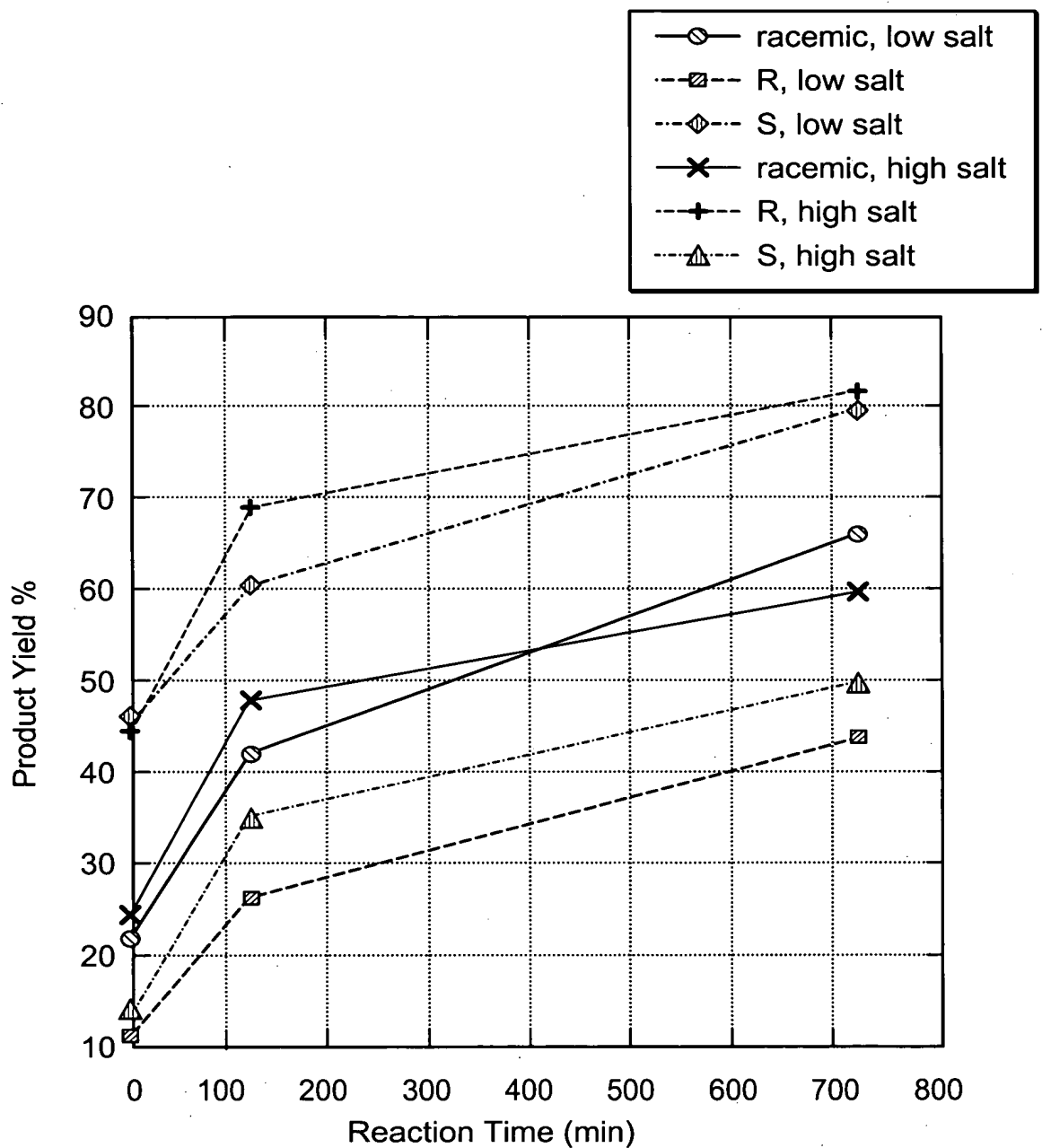


FIG. 42D



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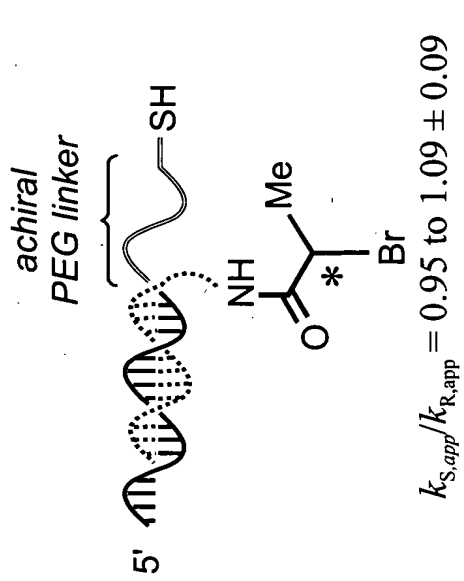


FIG. 43B

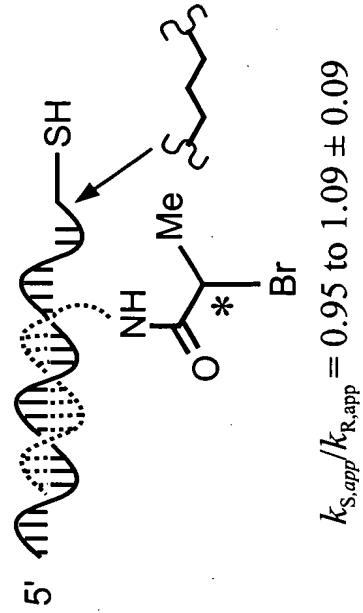


FIG. 43D

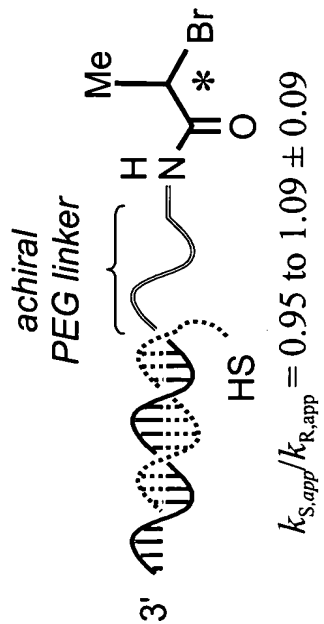


FIG. 43A

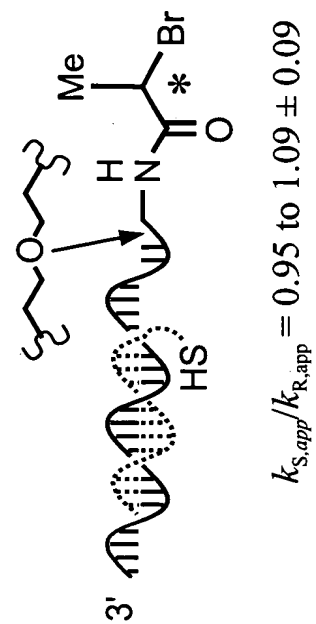


FIG. 43C

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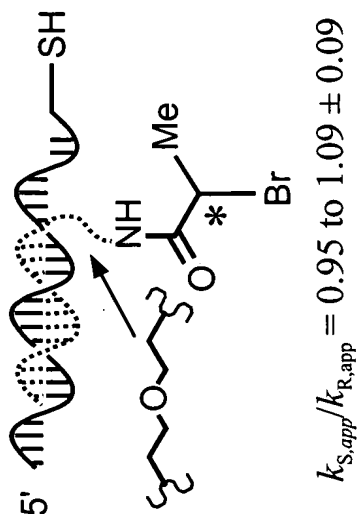


FIG. 43F

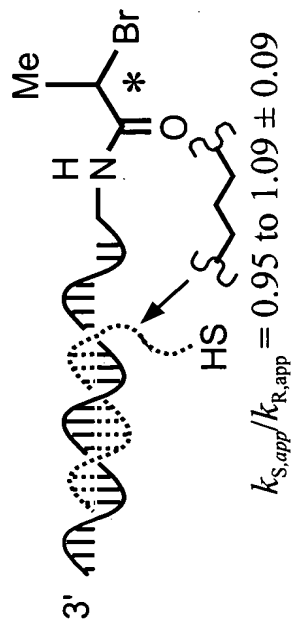


FIG. 43E

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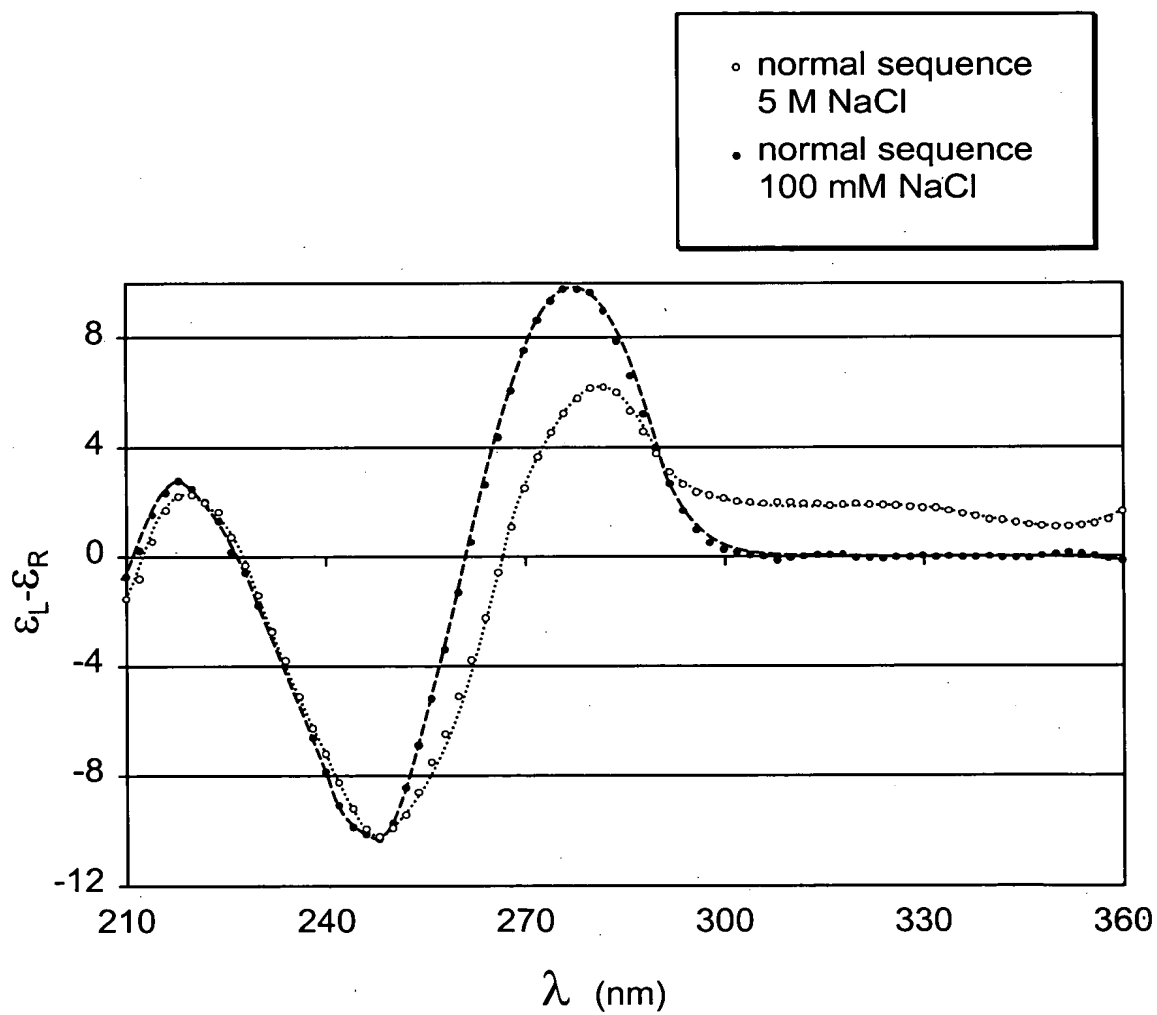


FIG. 44A

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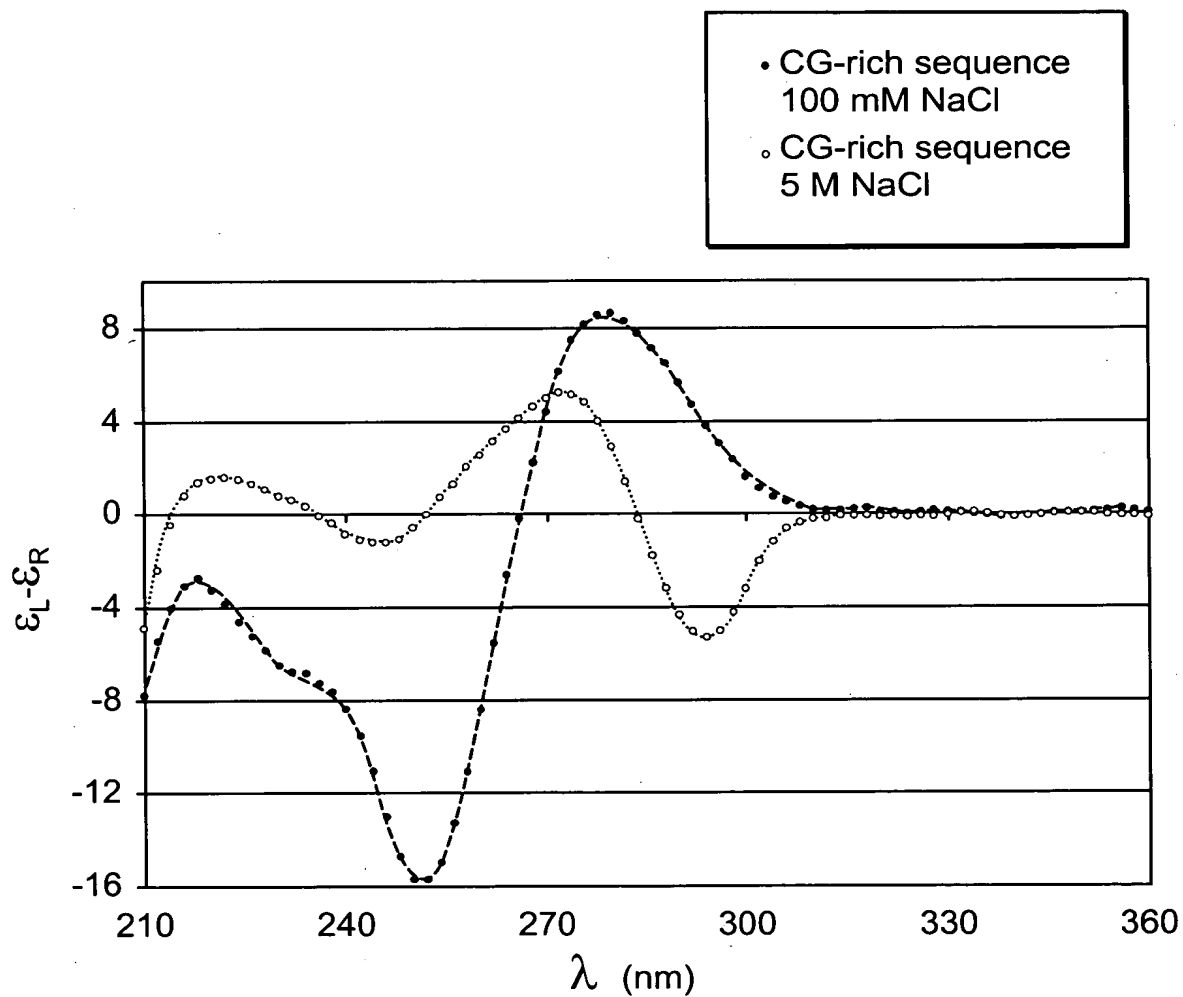


FIG. 44B

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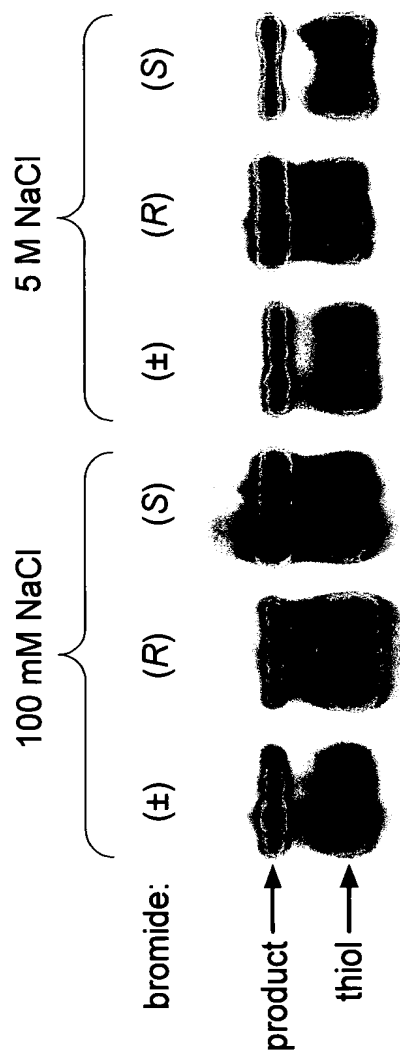


FIG. 45

|             |
|-------------|
| FIG.<br>46A |
| FIG.<br>46B |
| FIG.<br>46C |

FIG. 46

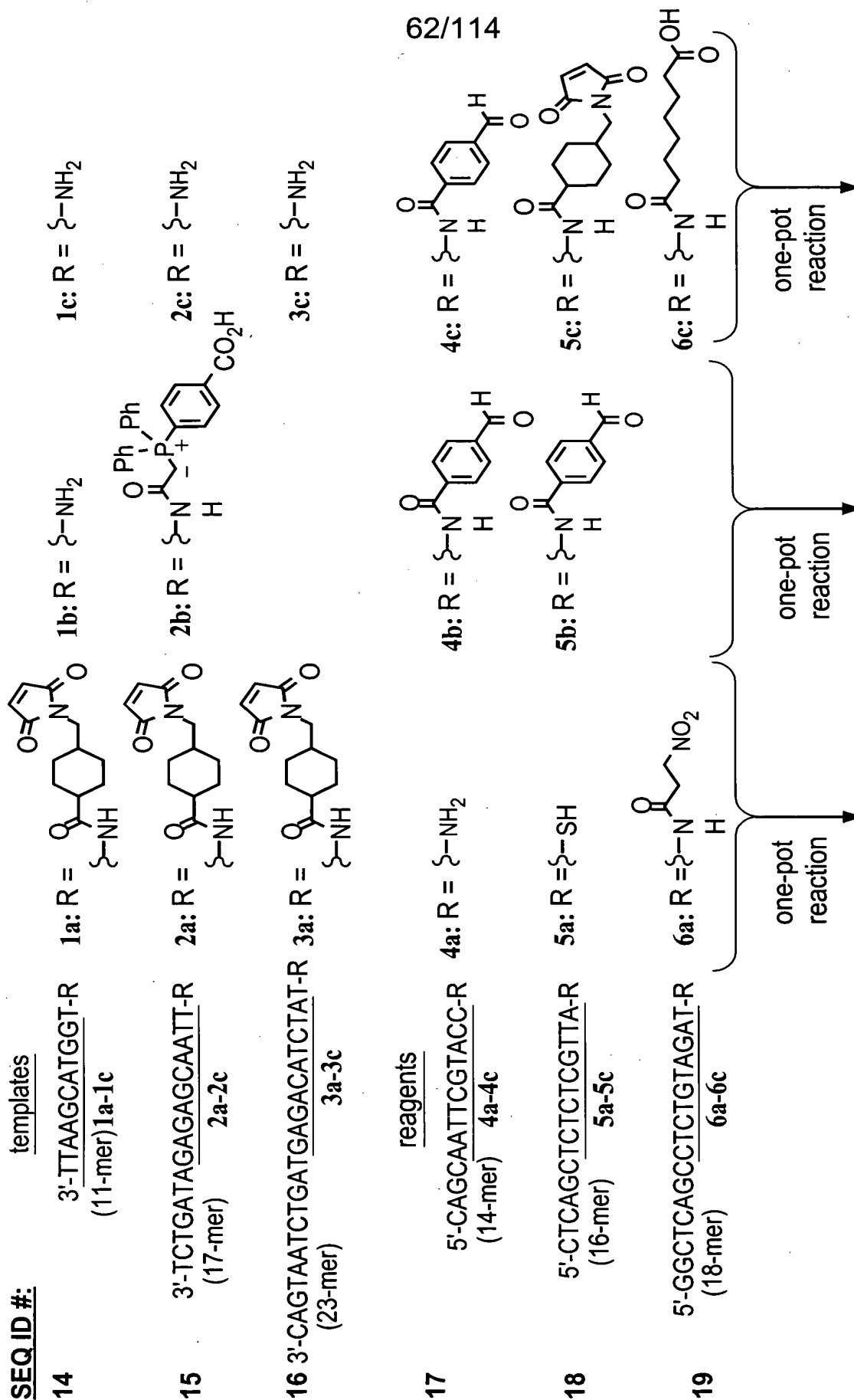


FIG. 46A

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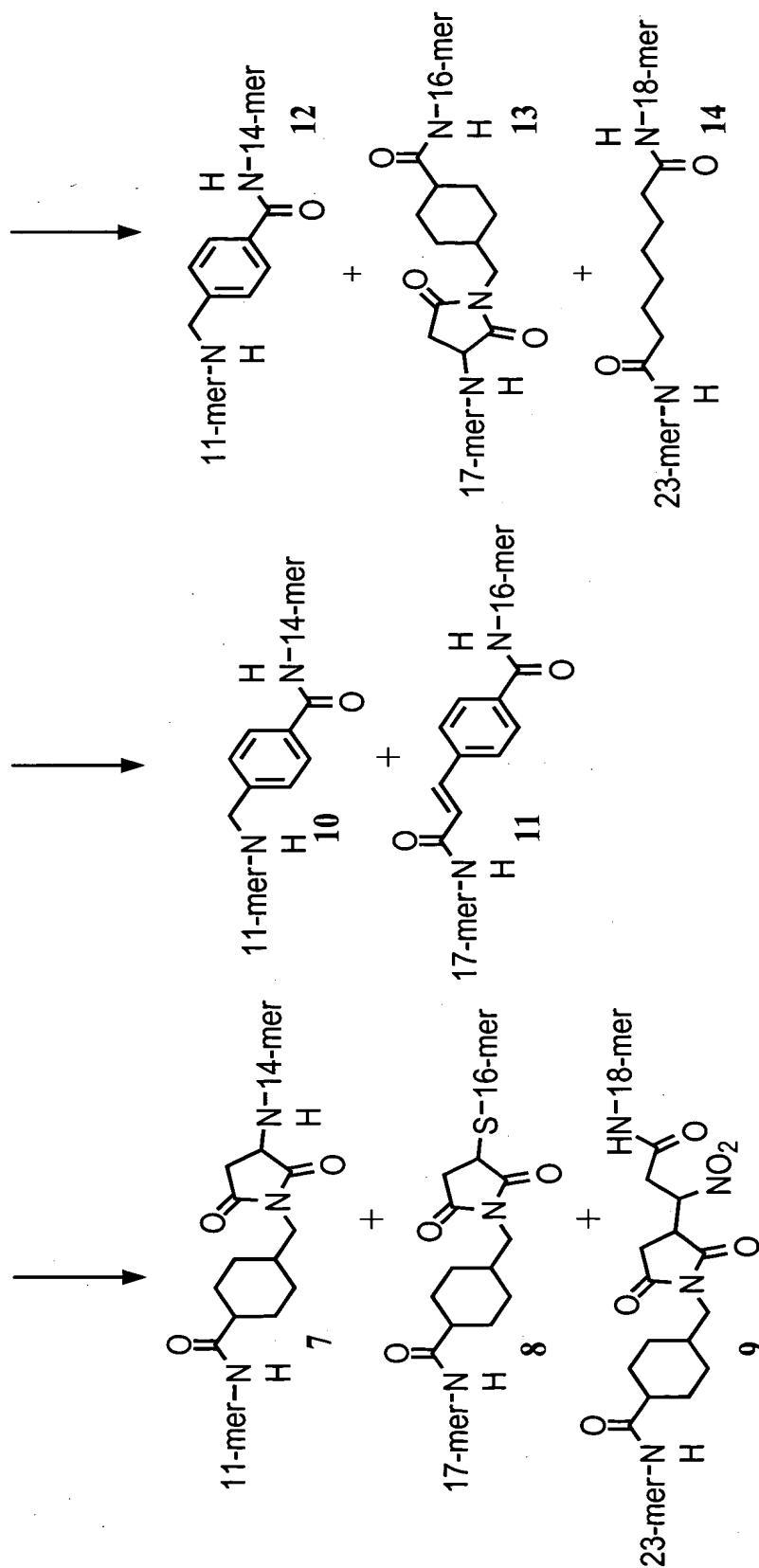


FIG. 46B

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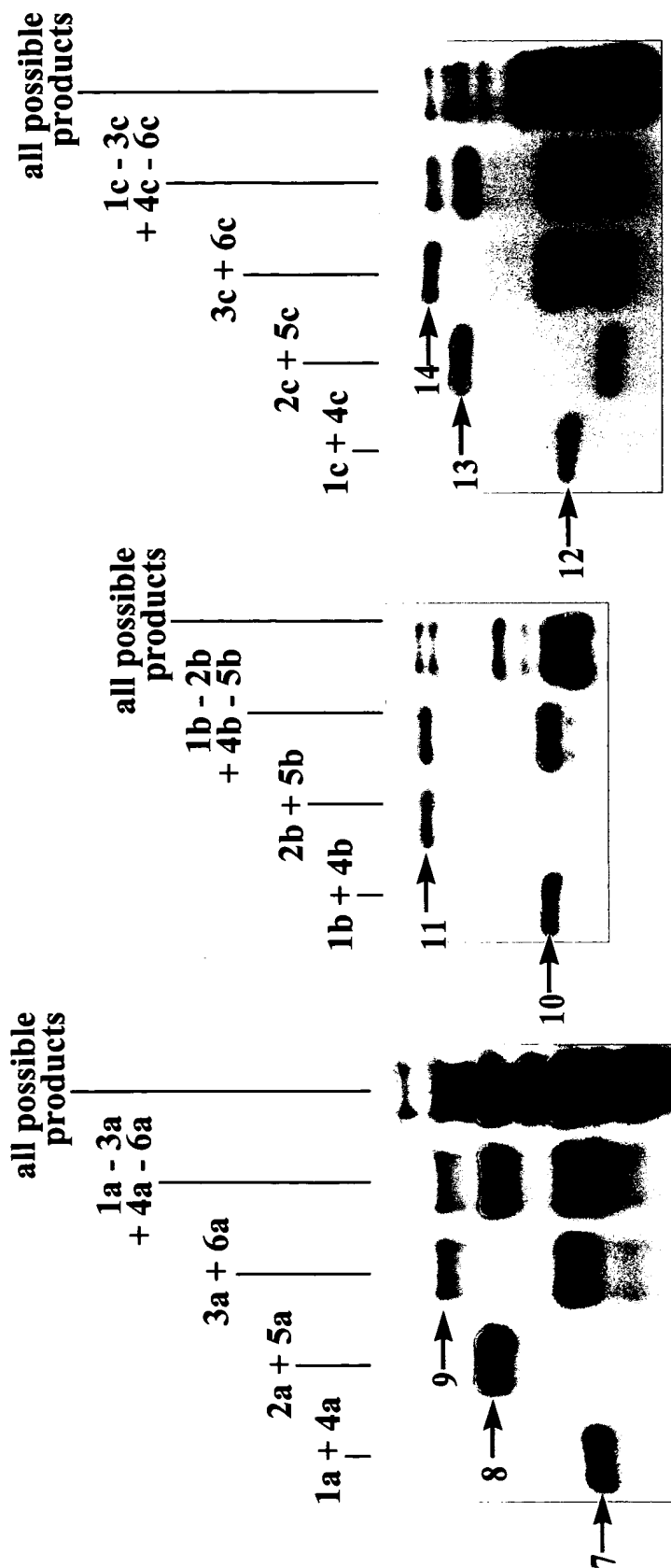


FIG. 46C



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SEQ ID NO:                      templates

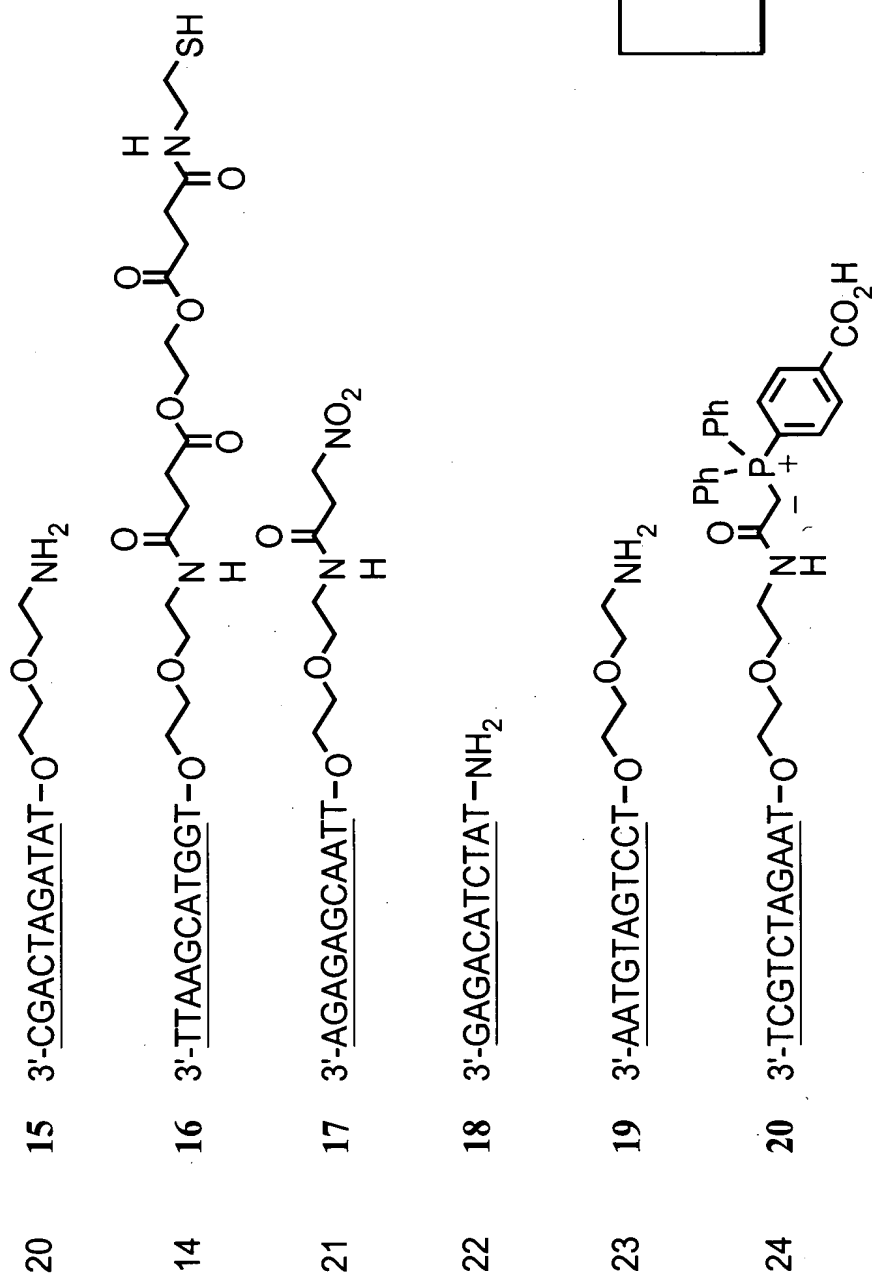


FIG. 47A

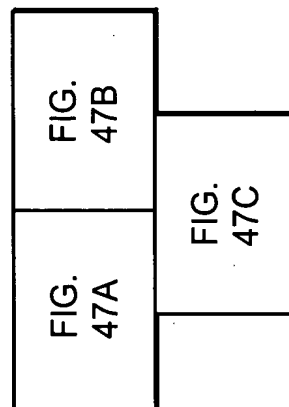


FIG. 47

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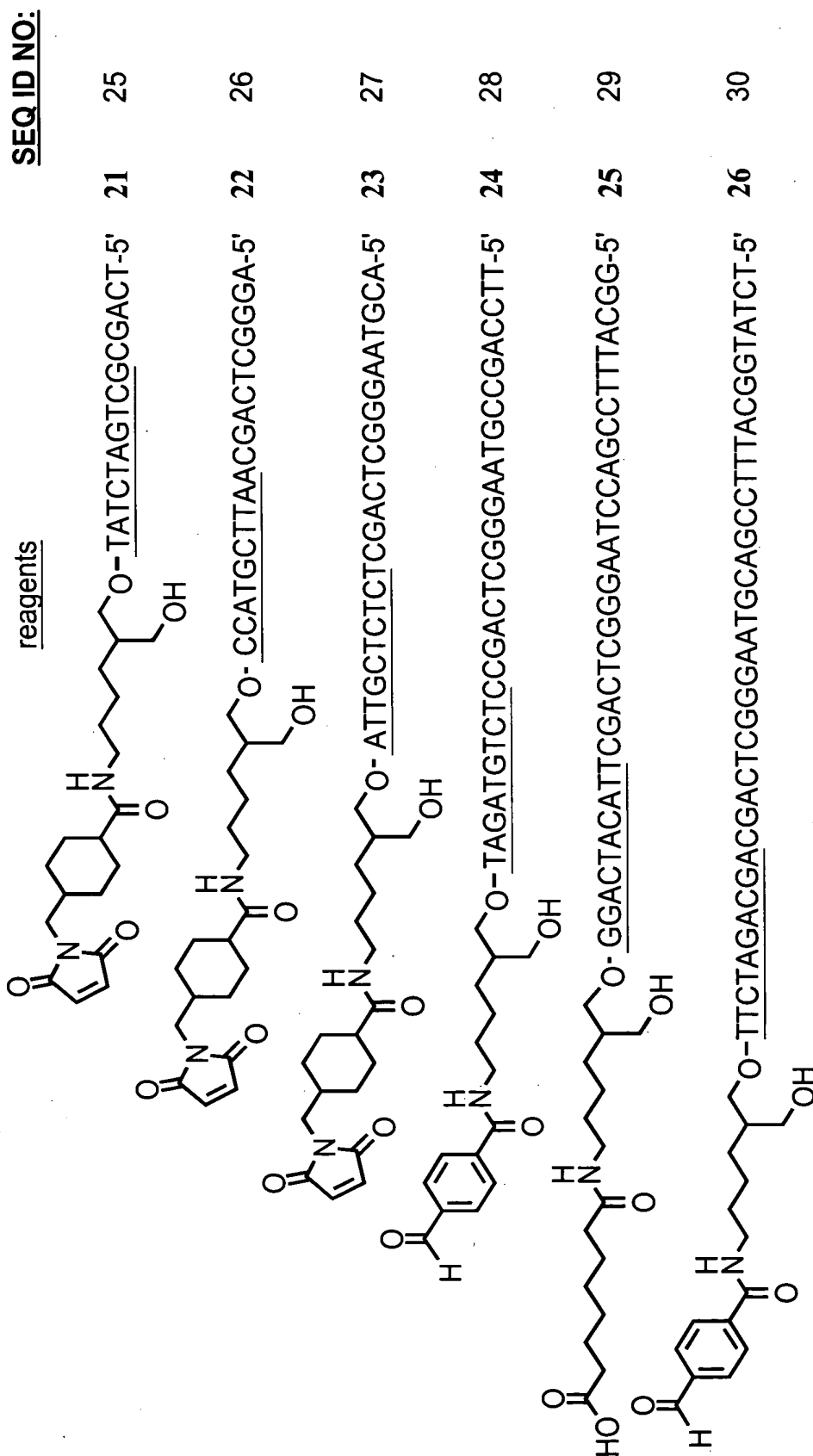


FIG. 47B

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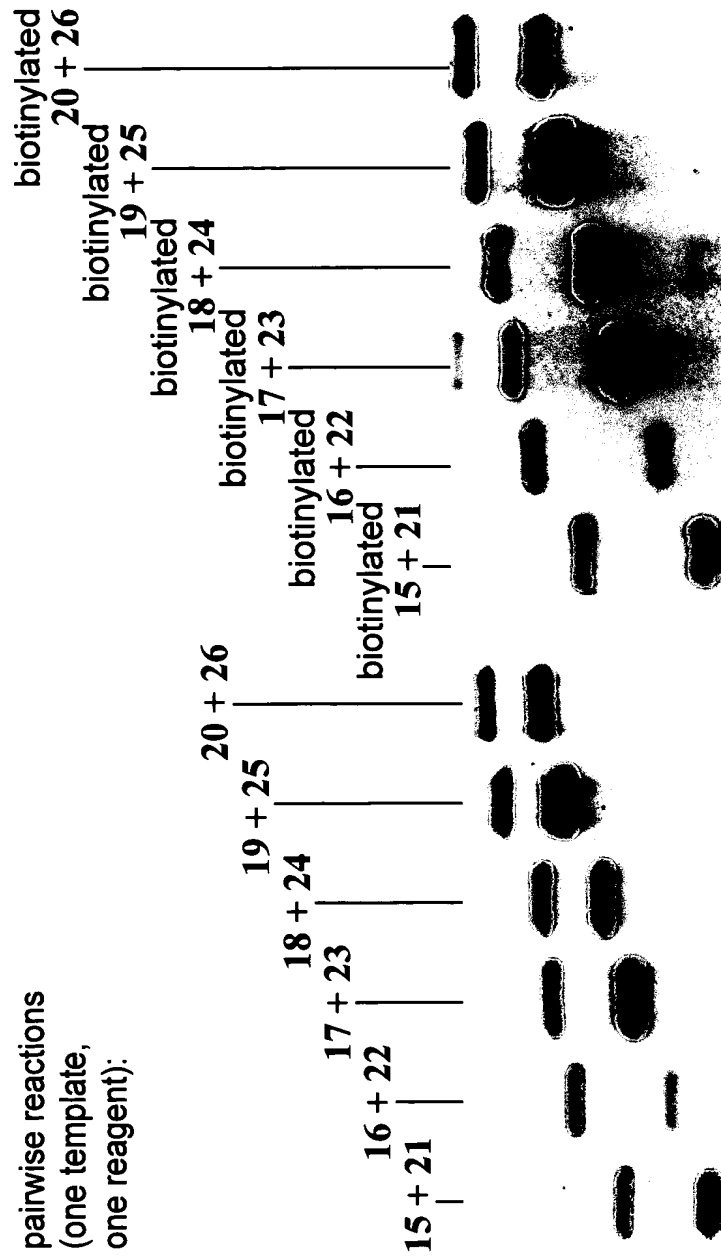
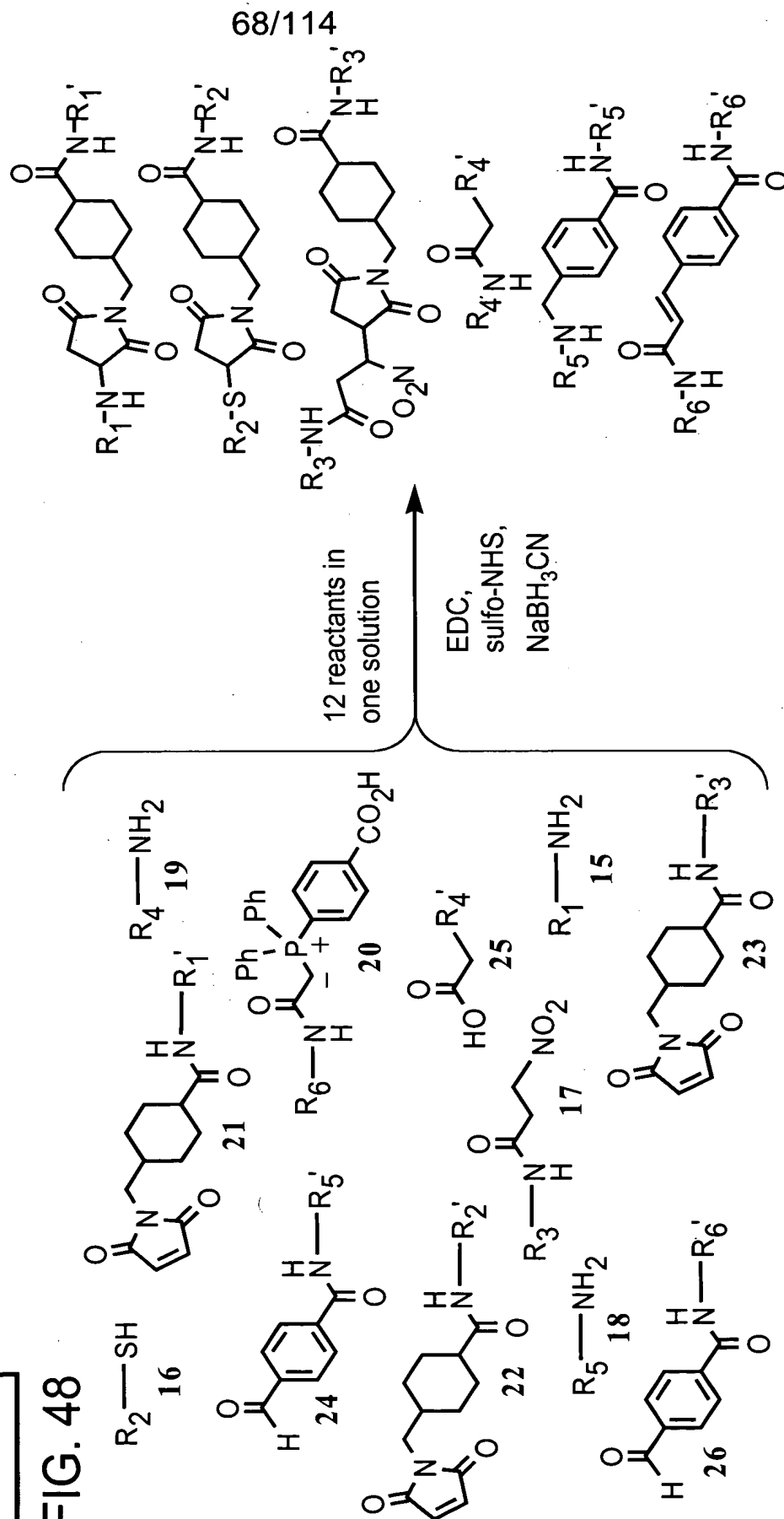


FIG. 47C

FIG. 48A

|          |
|----------|
| FIG. 48A |
| FIG. 48B |

FIG. 48



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one-pot reactions containing one biotinylated template (15, 16, 17, 18, 19, or 20)  
 + five non-biotinylated templates (out of 15-20) + six reagents (21-26)

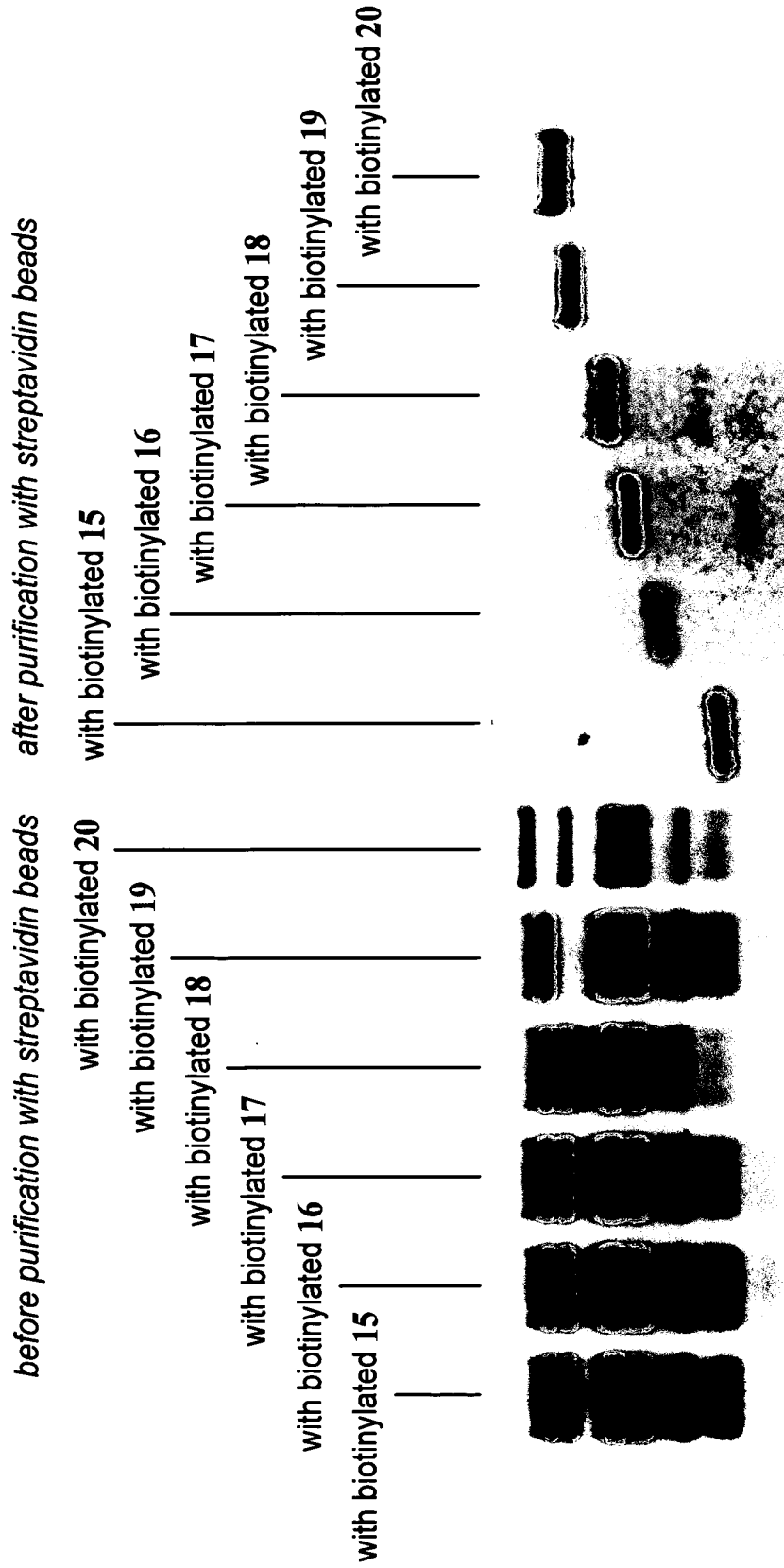


FIG. 48B

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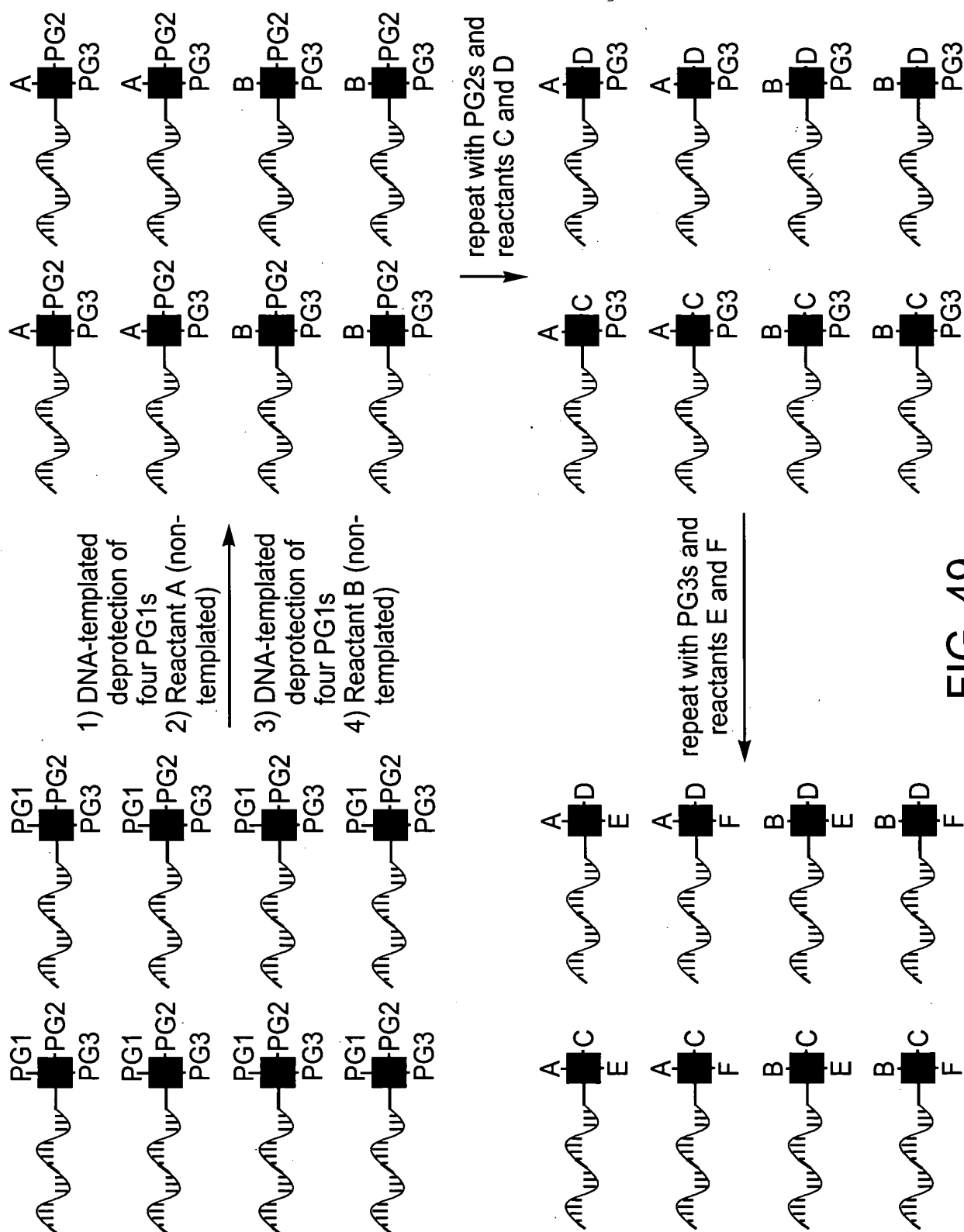
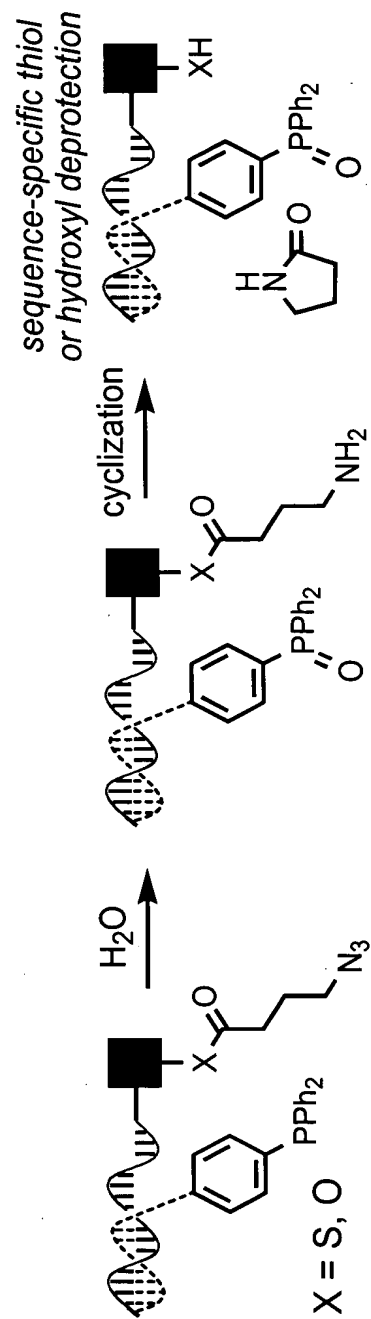
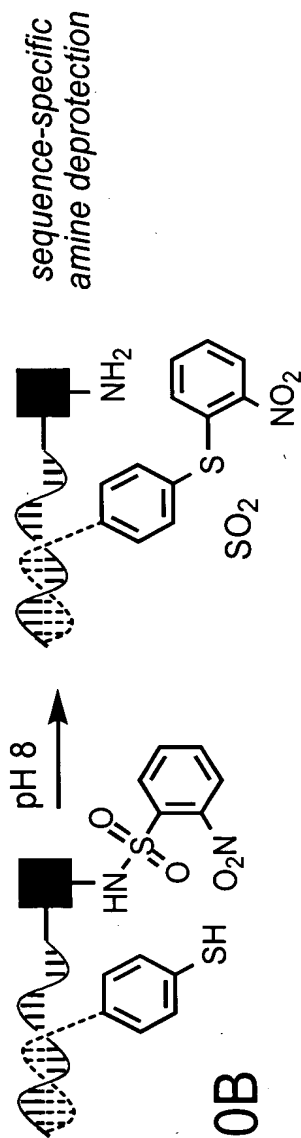
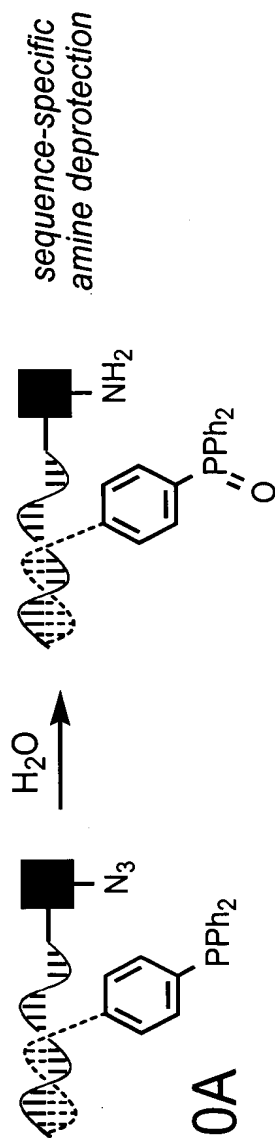


FIG. 49

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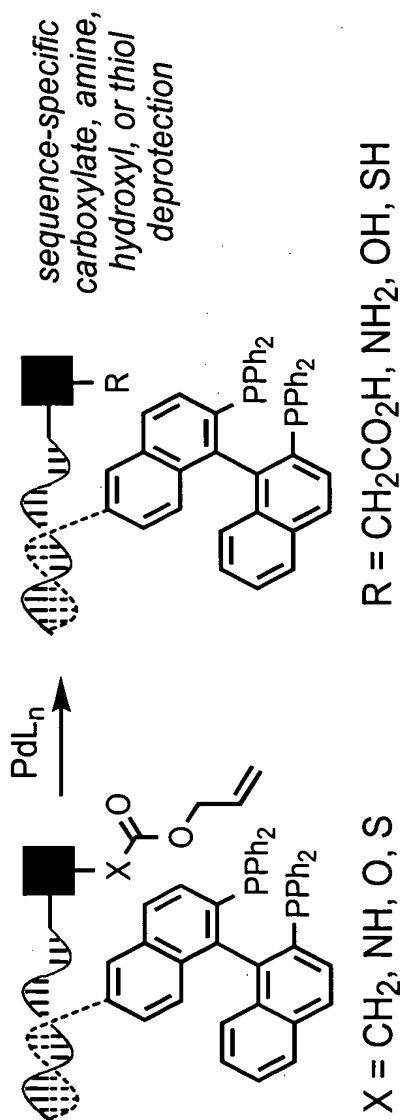


FIG. 50D

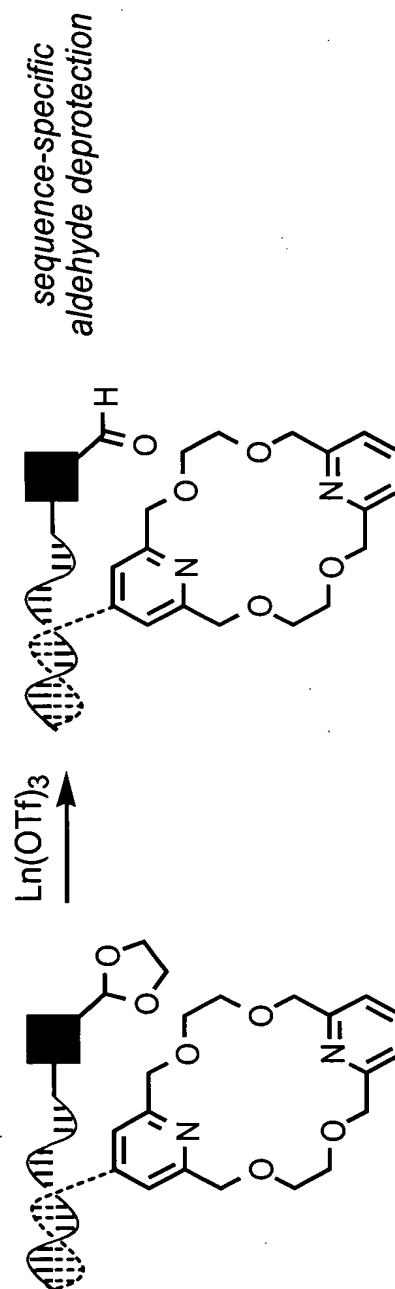
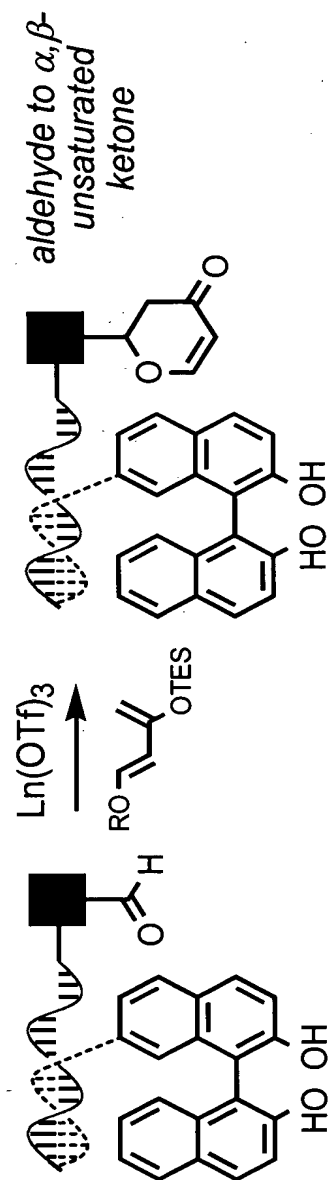
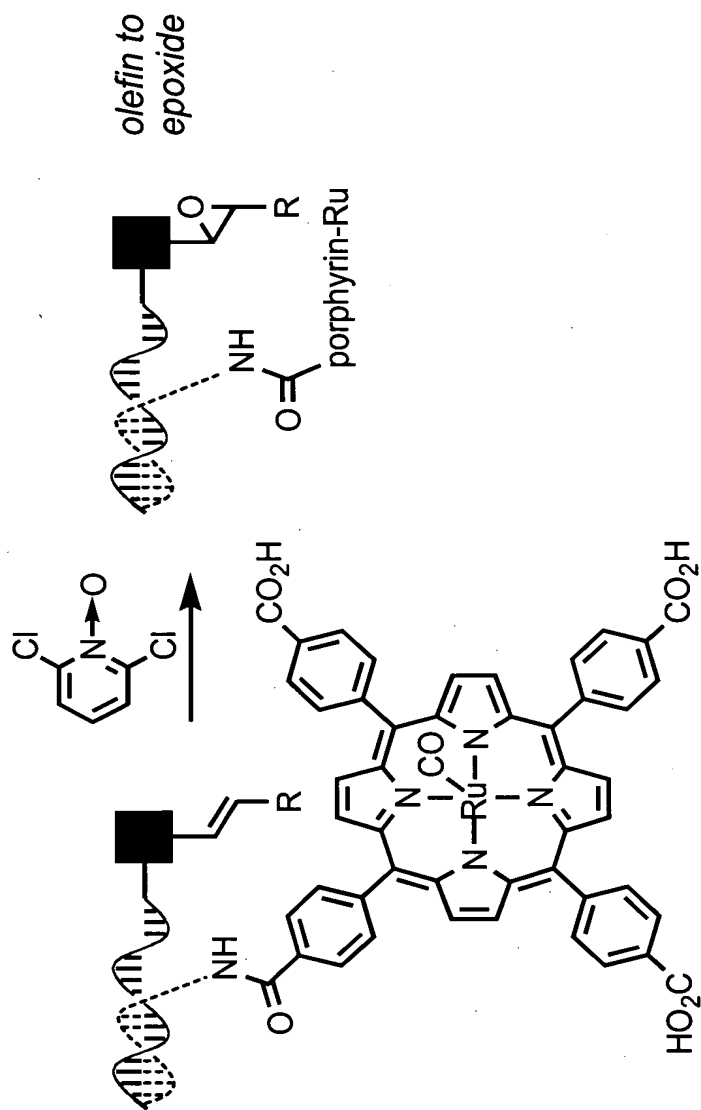


FIG. 50E



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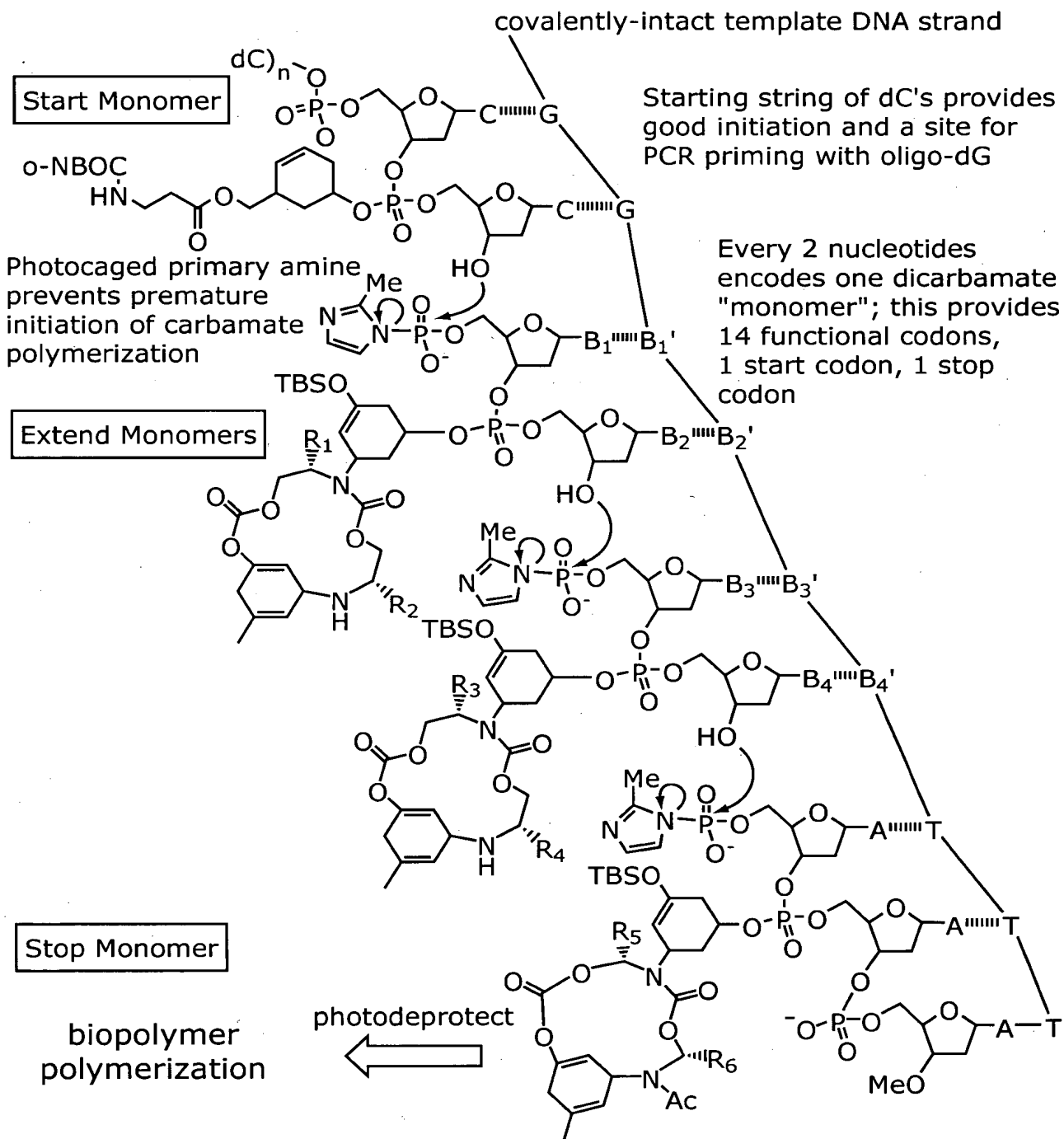


FIG. 52



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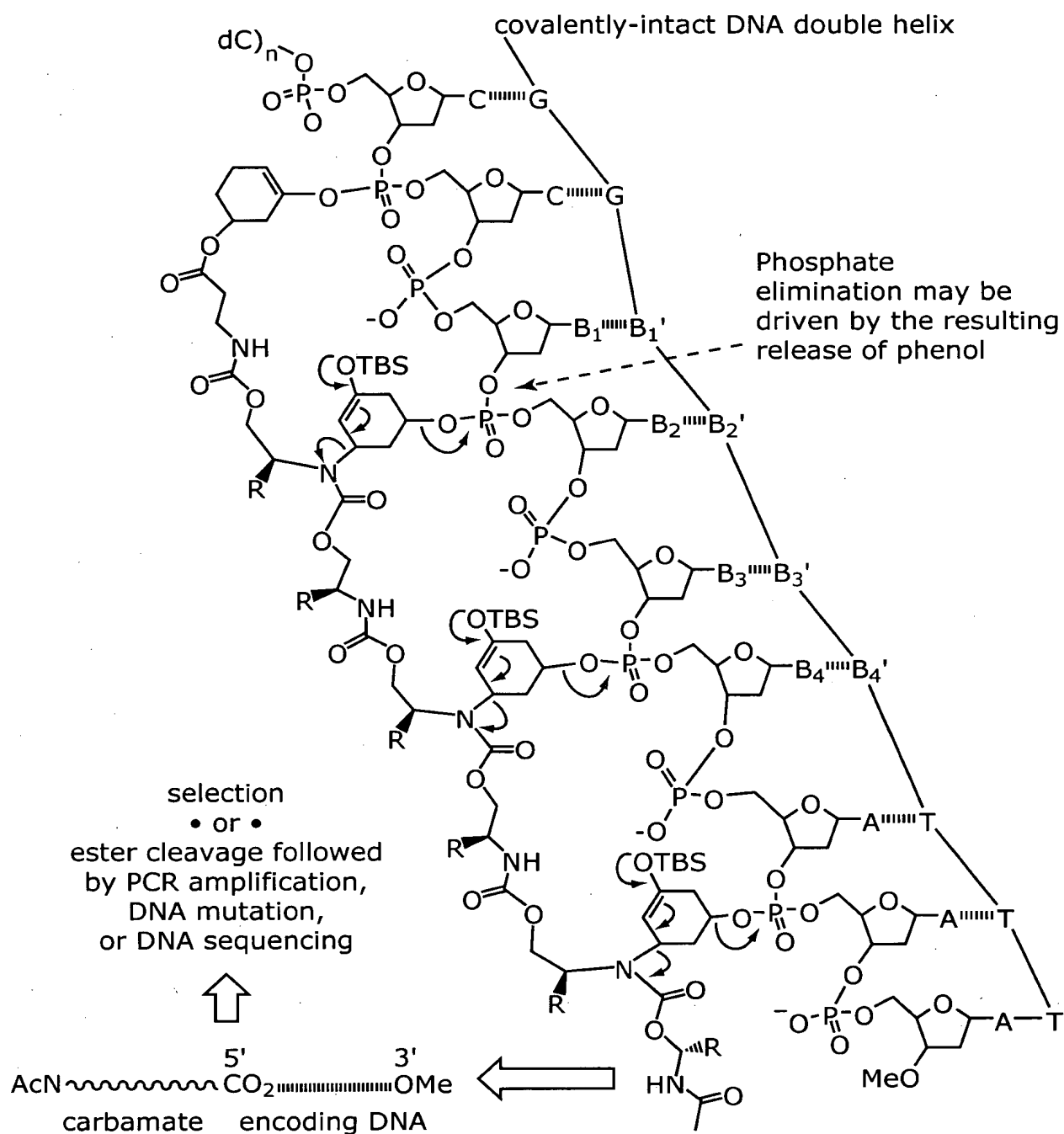


FIG. 54

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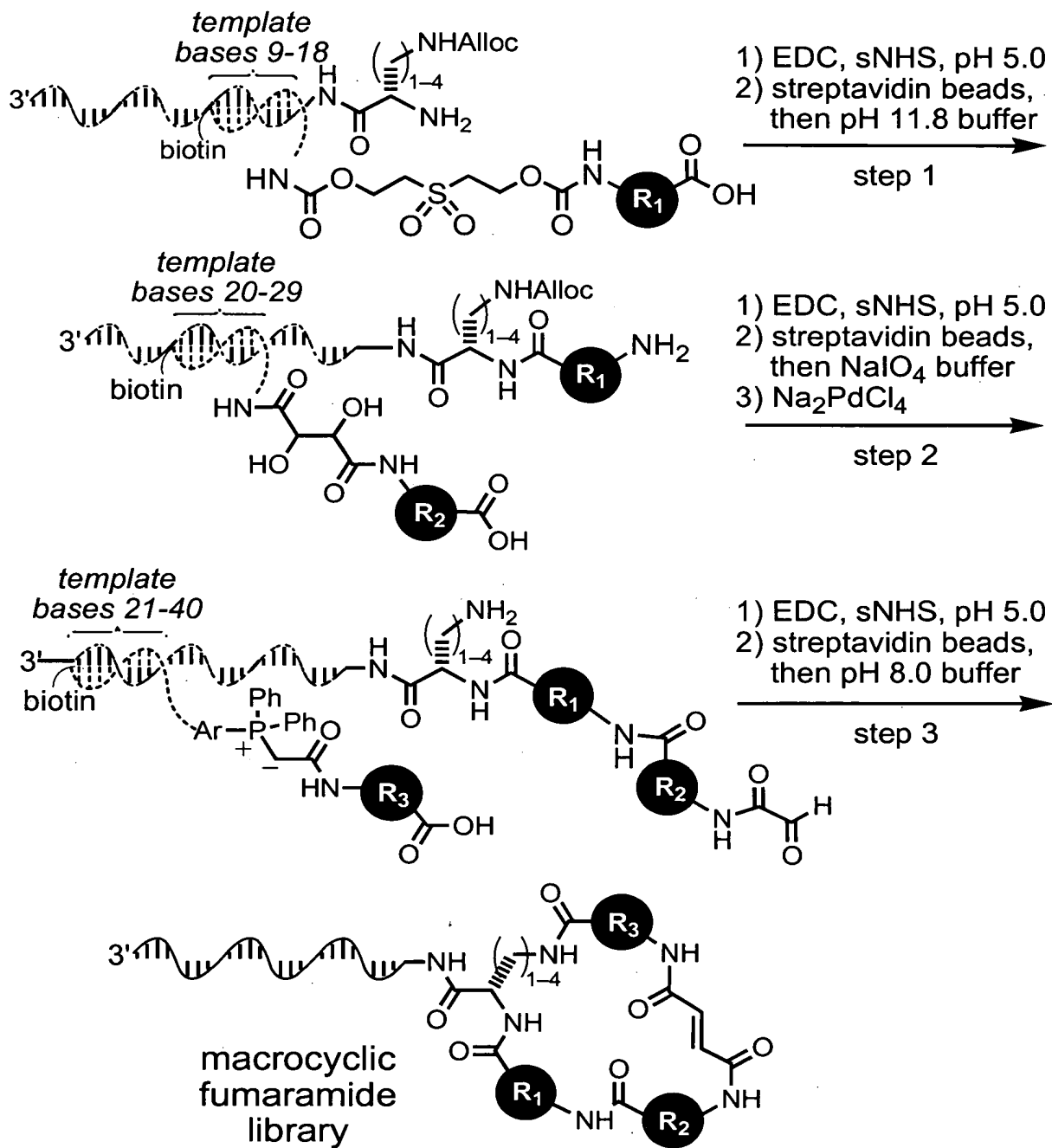
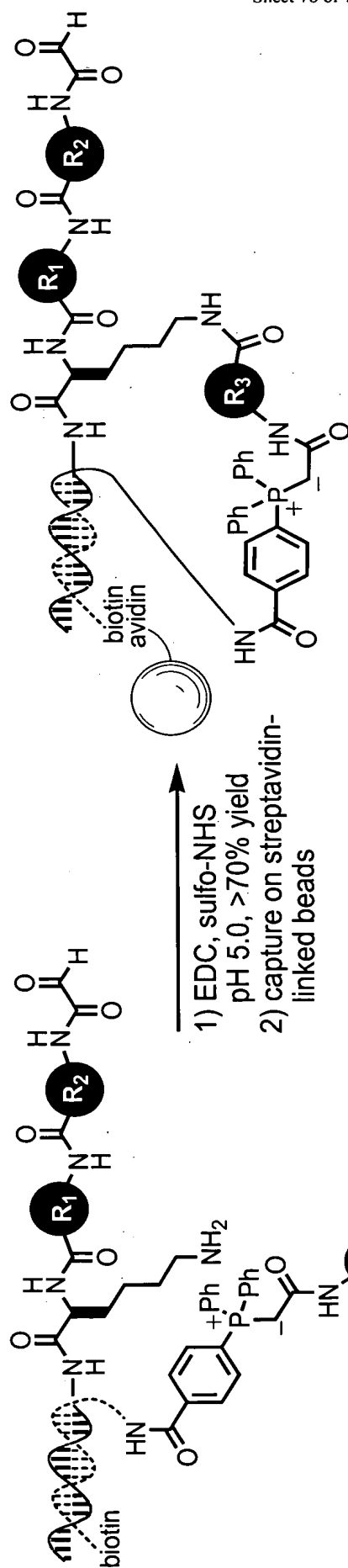


FIG. 55

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| R <sub>1</sub> | R <sub>2</sub> | R <sub>3</sub> | cyclization yield |
|----------------|----------------|----------------|-------------------|
| Gly            | Gly            | Ala            | ~90%              |
| Ala            | Ala            | Ala            | ~90%              |
| Ala            | (D)-Ala        | Ala            | ~90%              |
| Val            | Val            | Val            | ~90%              |
| Val            | Val            | Leu            | ~90%              |
| Val            | (D)-Val        | Val            | ~80%              |
| Val            | (D)-Val        | Leu            | ~80%              |
| Phe            | Phe            | Ala            | ~80%              |
| Phe            | Phe            | Leu            | ~80%              |
| GABA           | GABA           | β-Ala          | ~80%              |
| Phe            | Phe            | Phe            | ~60%              |

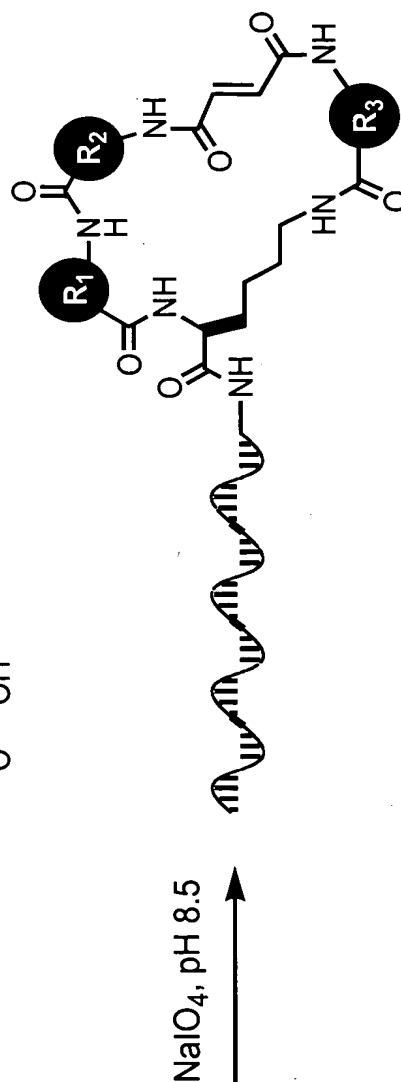
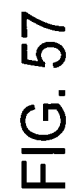


FIG. 56



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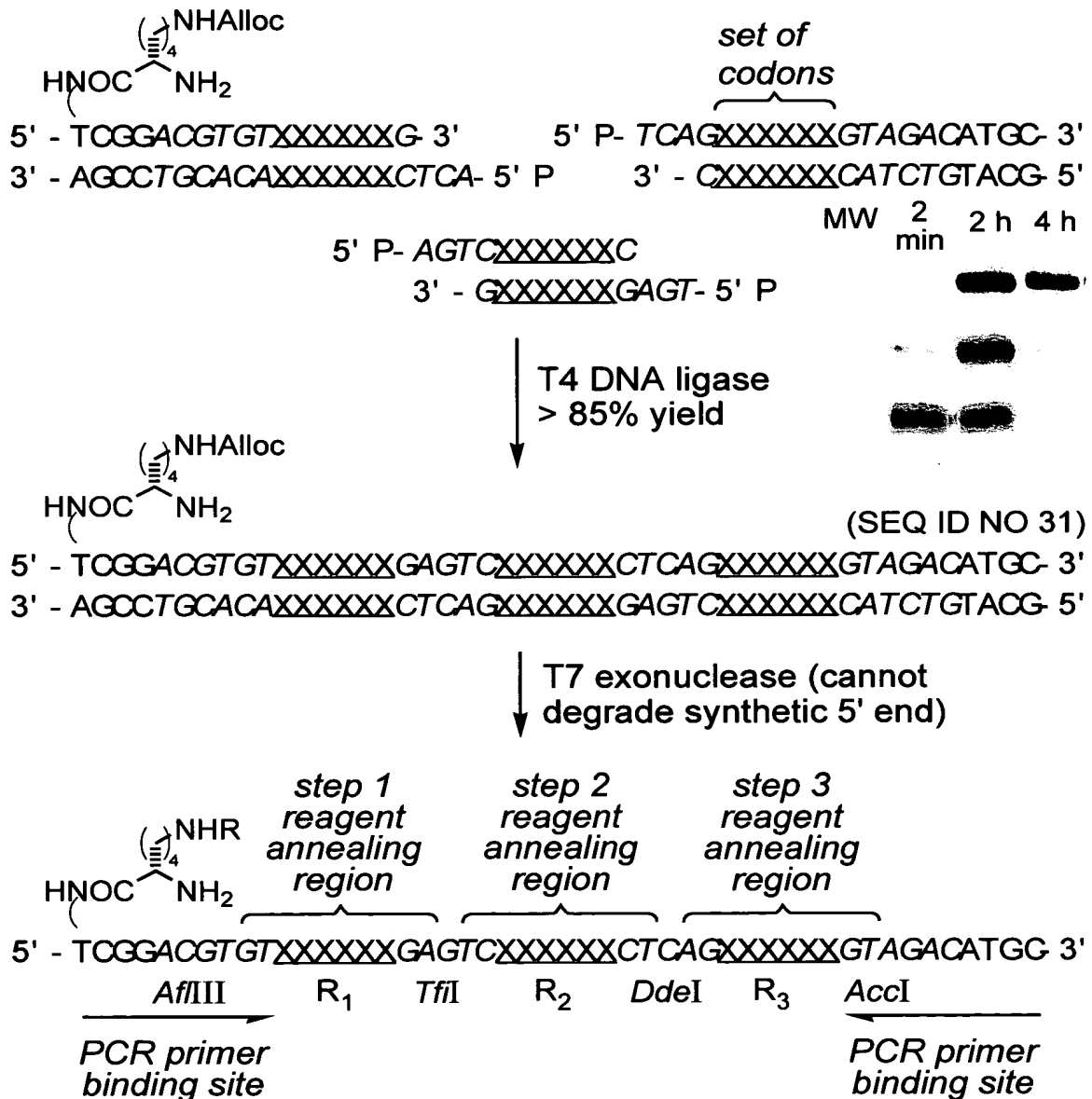


FIG. 58



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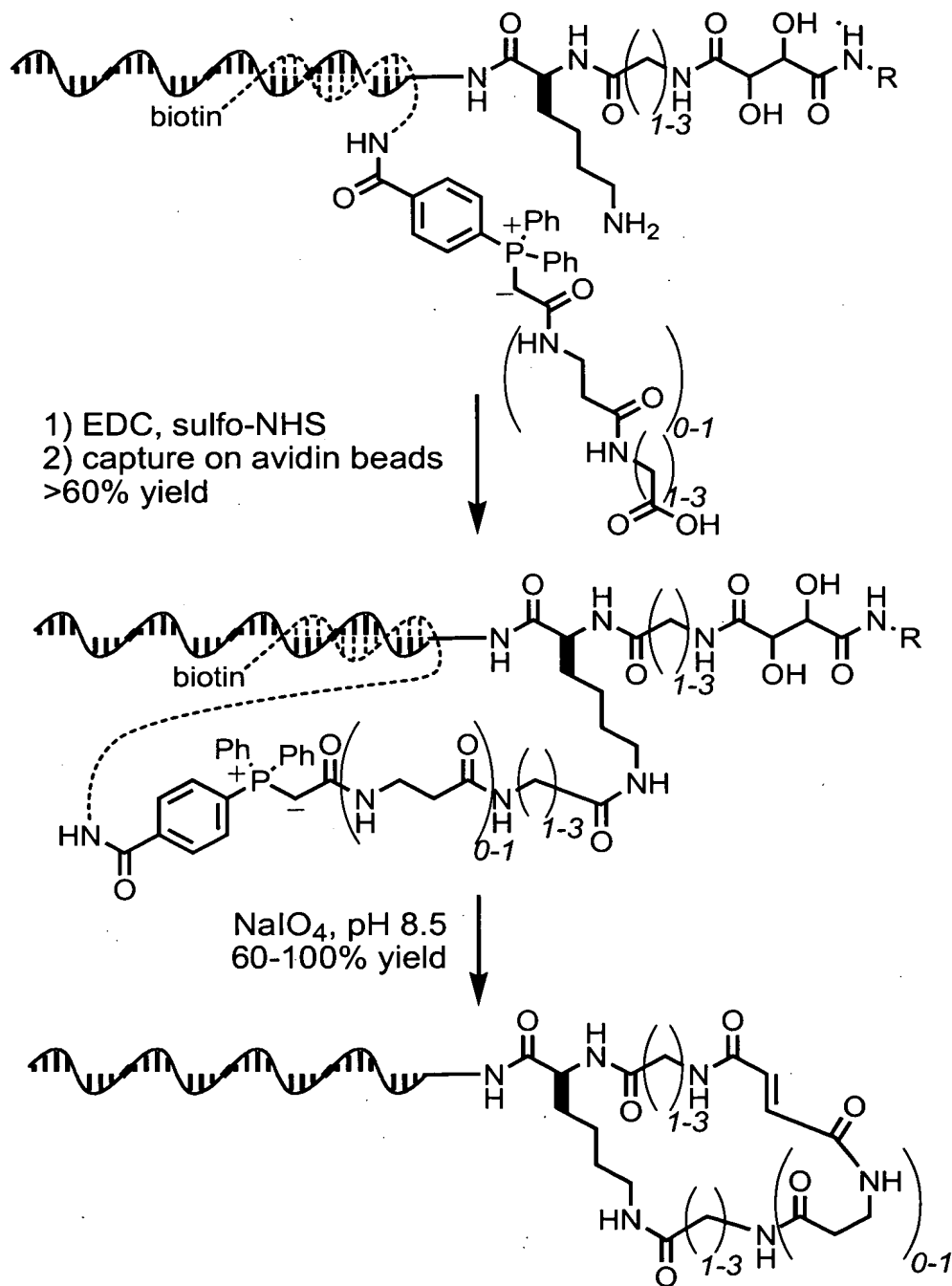
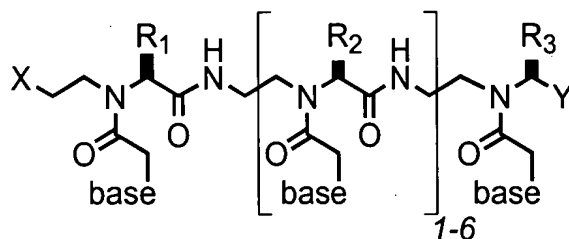


FIG. 59

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X, Y = groups for coupling (see Fig. 1)

R =

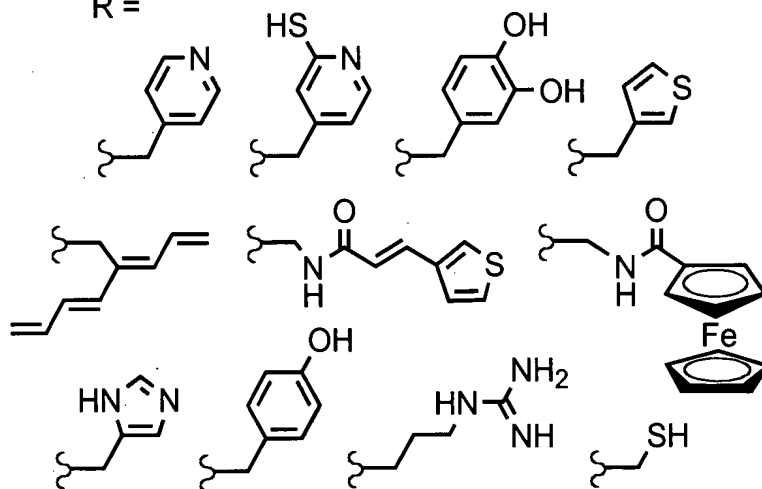


FIG. 60

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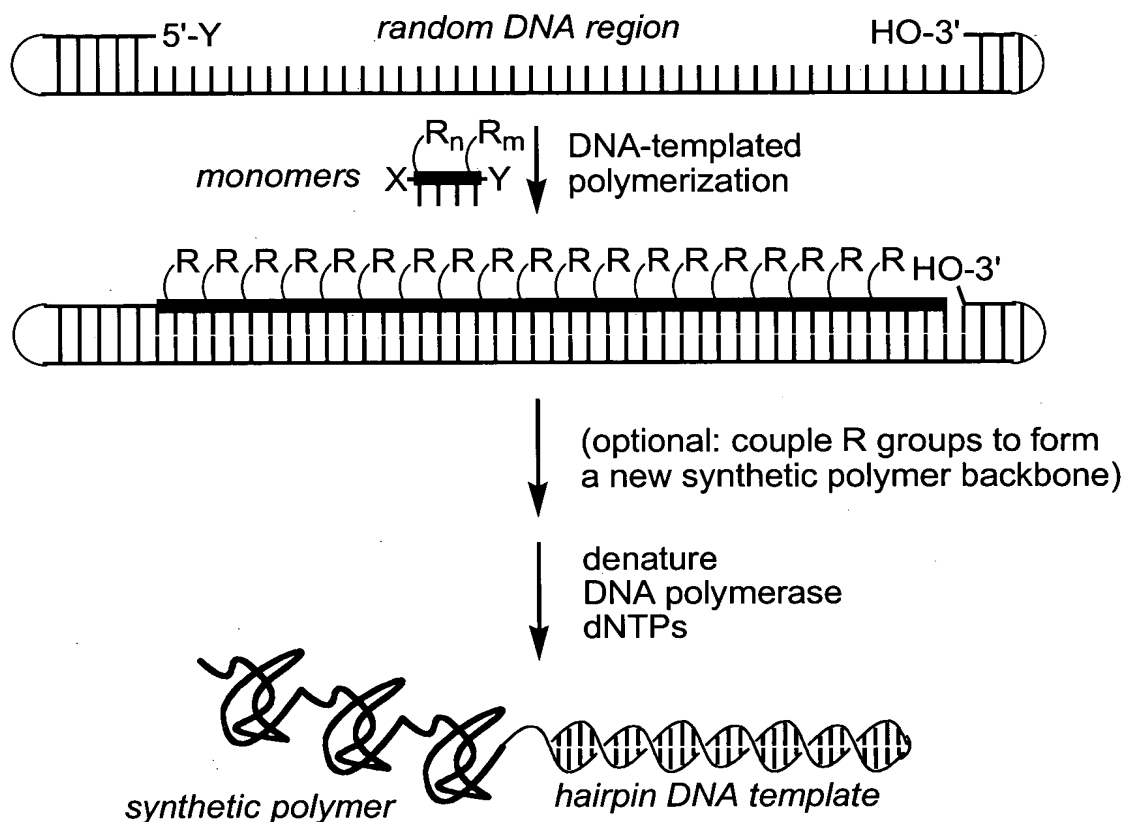


FIG. 61

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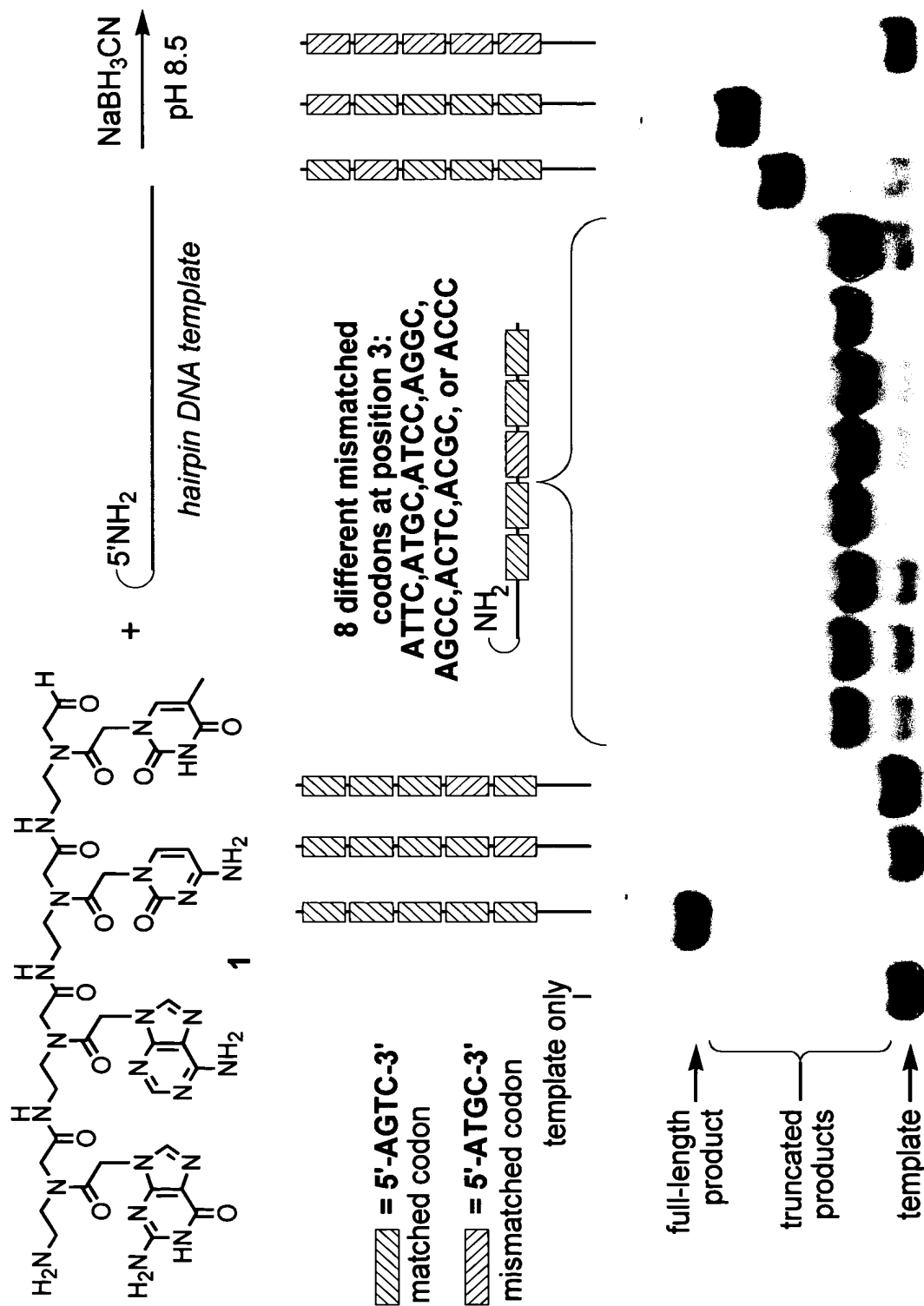


FIG. 62

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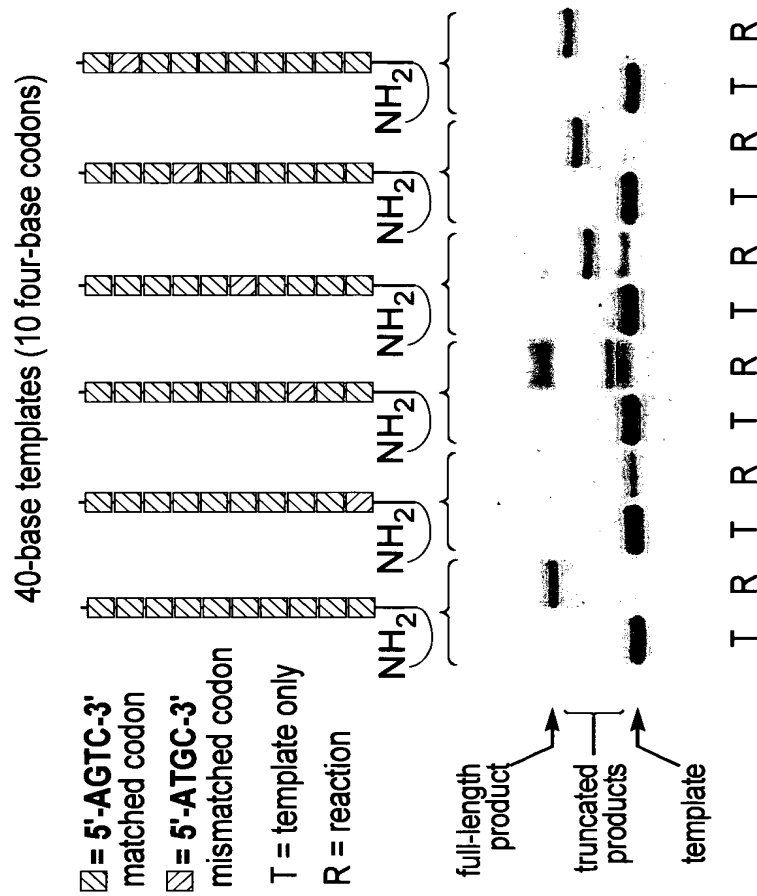


FIG. 63

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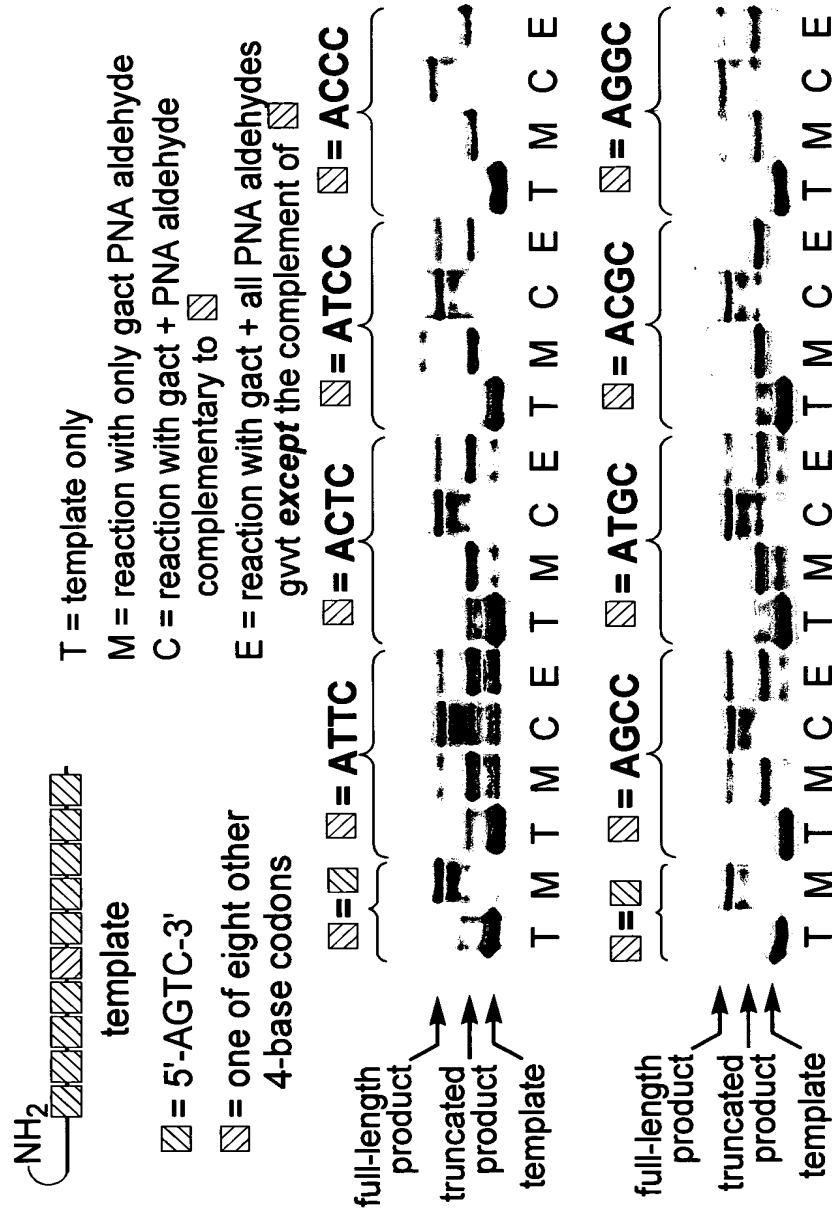
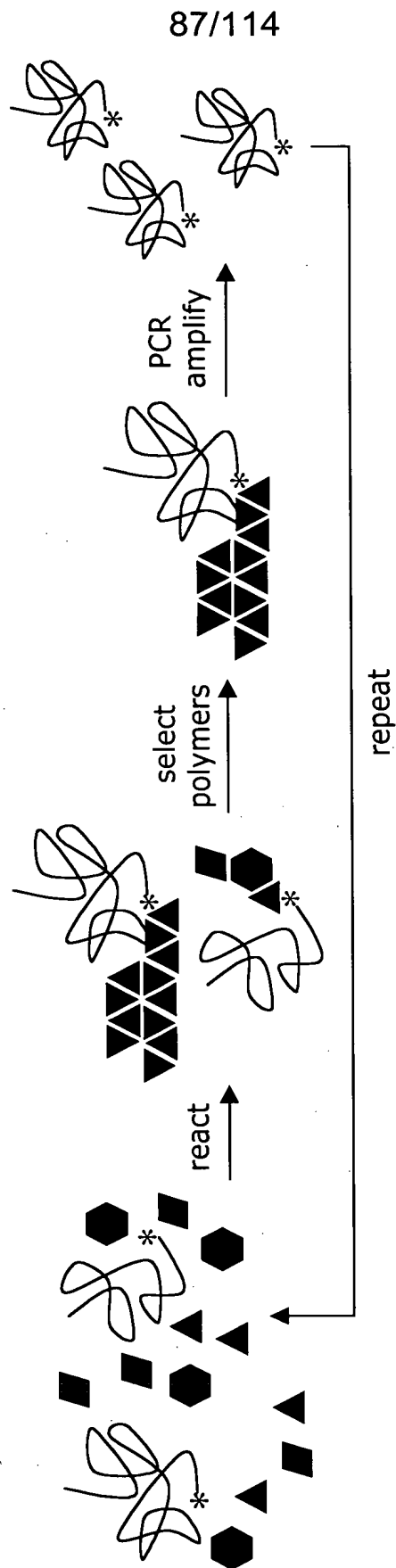


FIG. 64

## Evolving Plastics

How can amplifiable information be translated into materials with specific properties (e.g., plastics)?

- Nucleic acids can fold into complex structures



### Requirements:

- Linkage between information and product: need living polymerization
- Selection for desired materials: gel electrophoresis, sedimentation, mechanical sorting, solvent partitioning
- Chemical compatibility with DNA: stability in water

FIG. 65A

## Evolving Plastics

Ring-opening metathesis polymerization (ROMP, R. Grubbs) is mediated by a ruthenium catalyst  
ROMP is aqueous-compatible and is a living polymerization

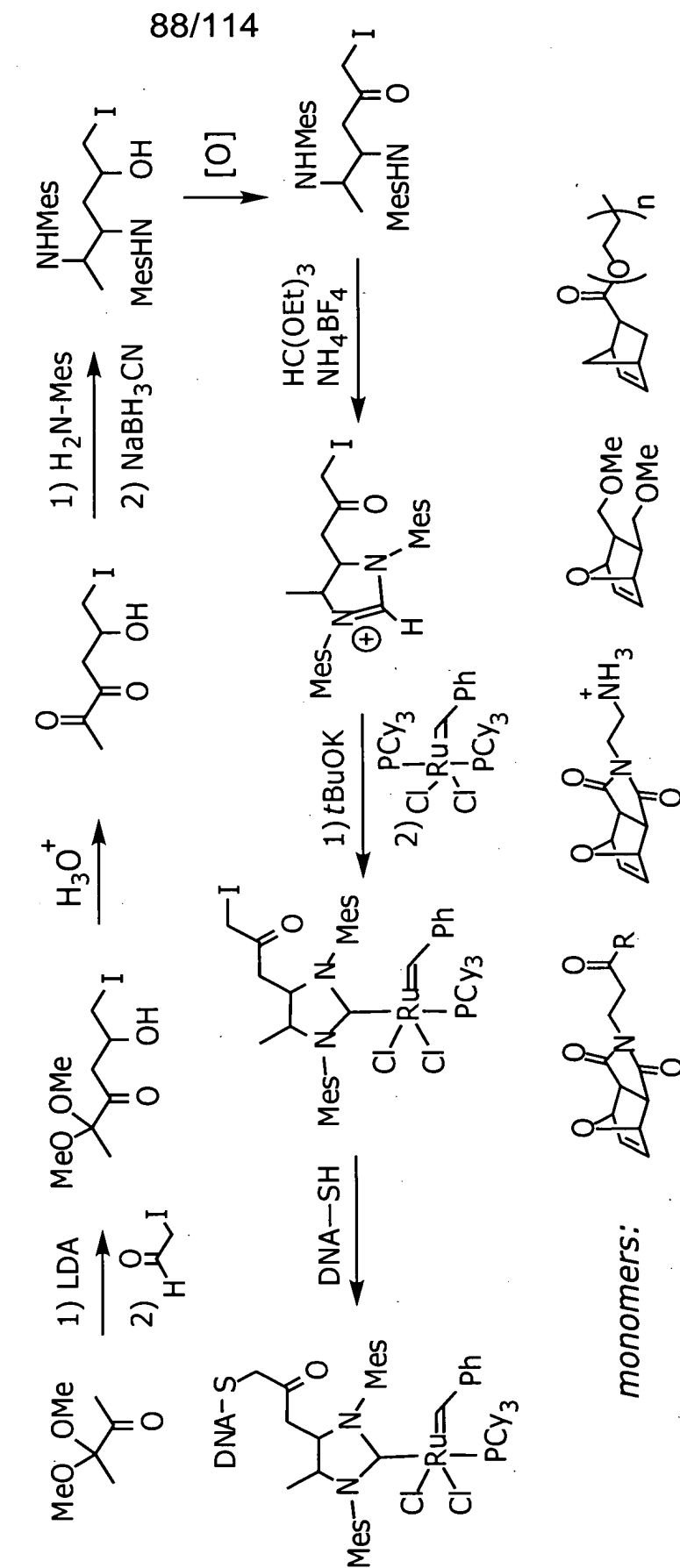
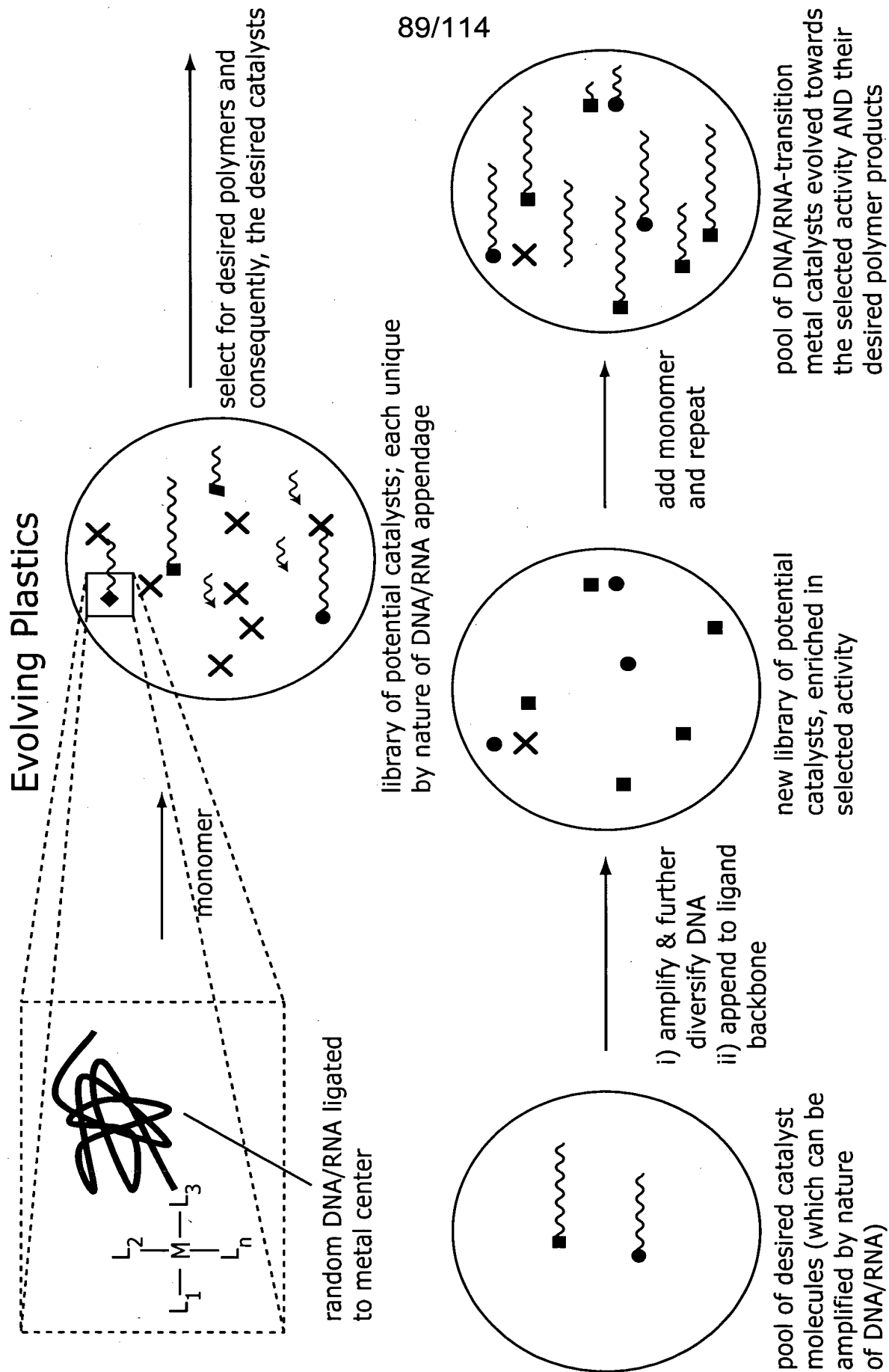
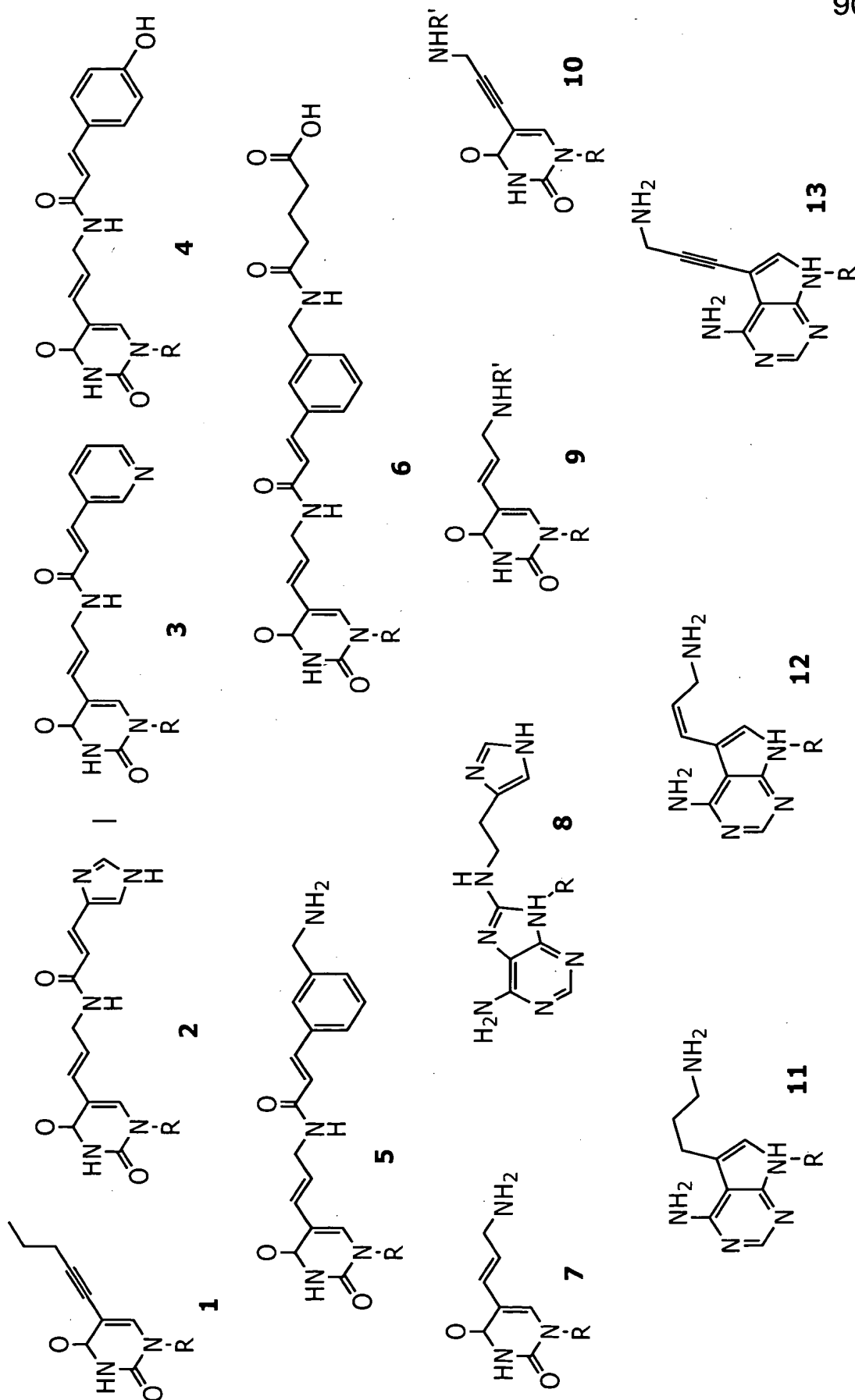


FIG. 65B





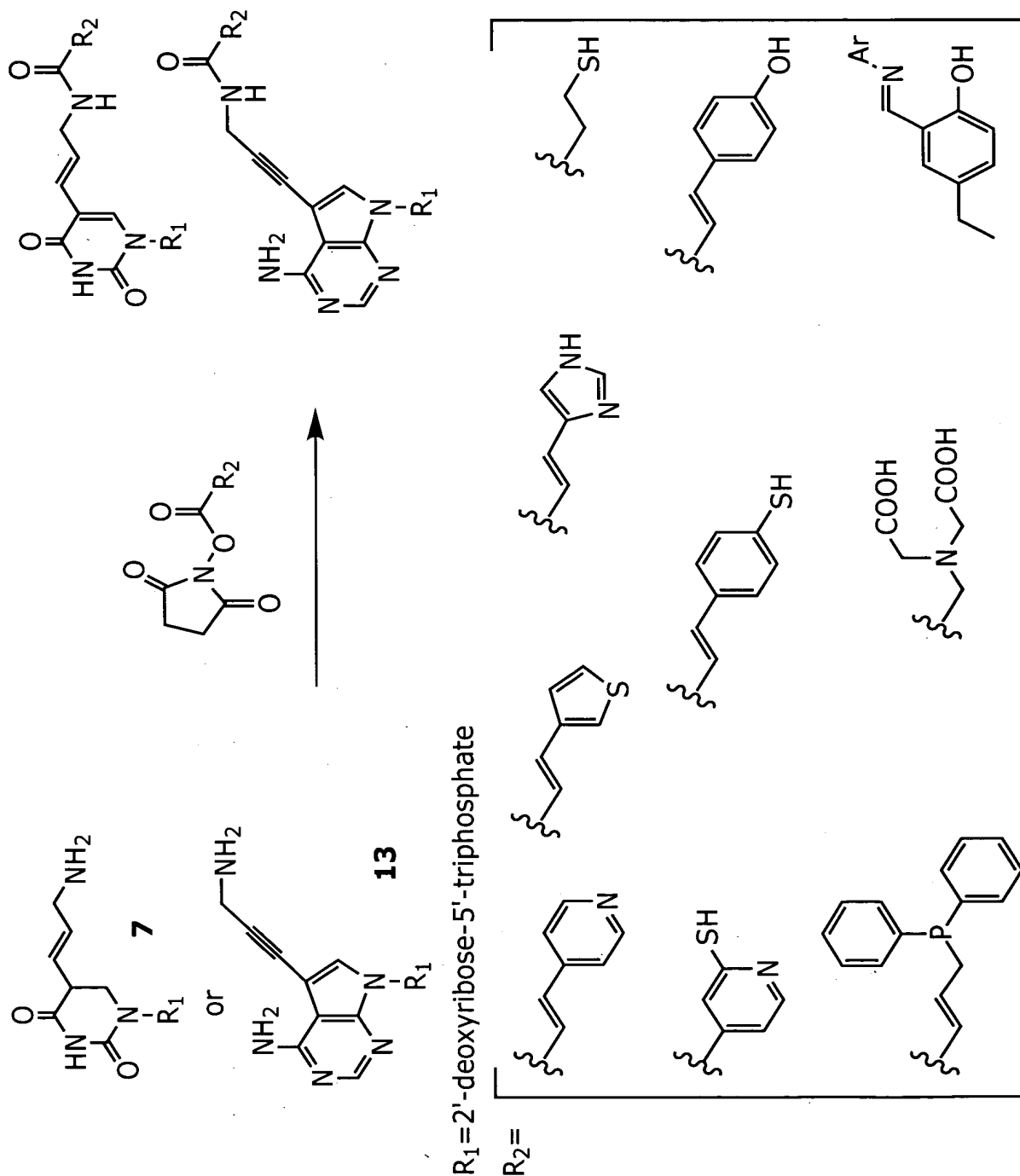
**FIG. 66**



R=2'-deoxyribonucleotide 5'-triphosphate

FIG. 67

FIG. 68



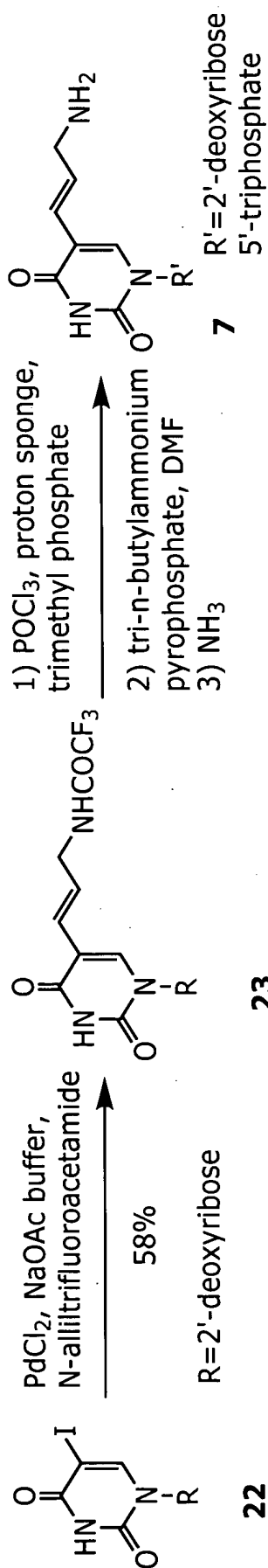


FIG. 69

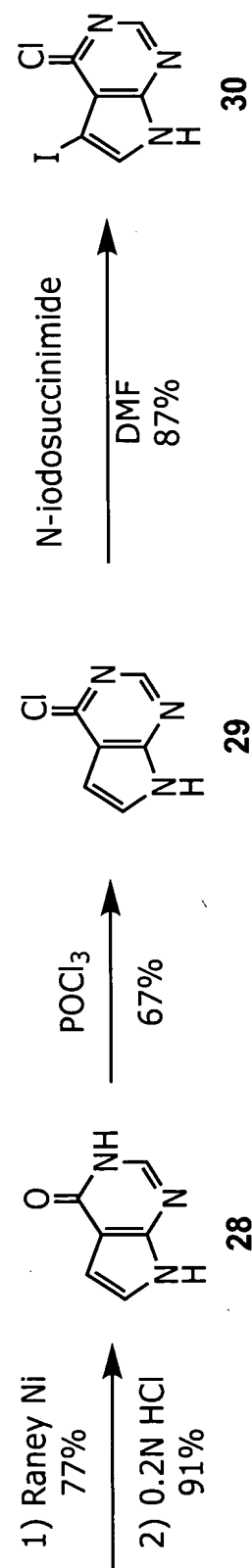
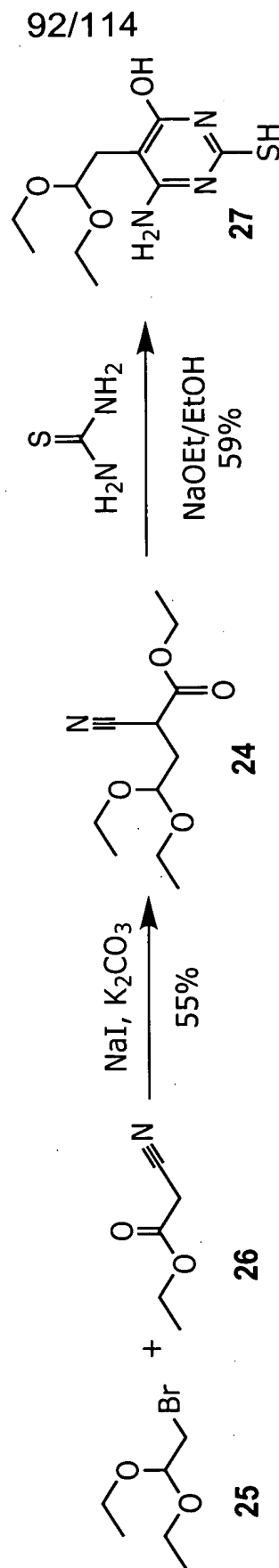


FIG. 70

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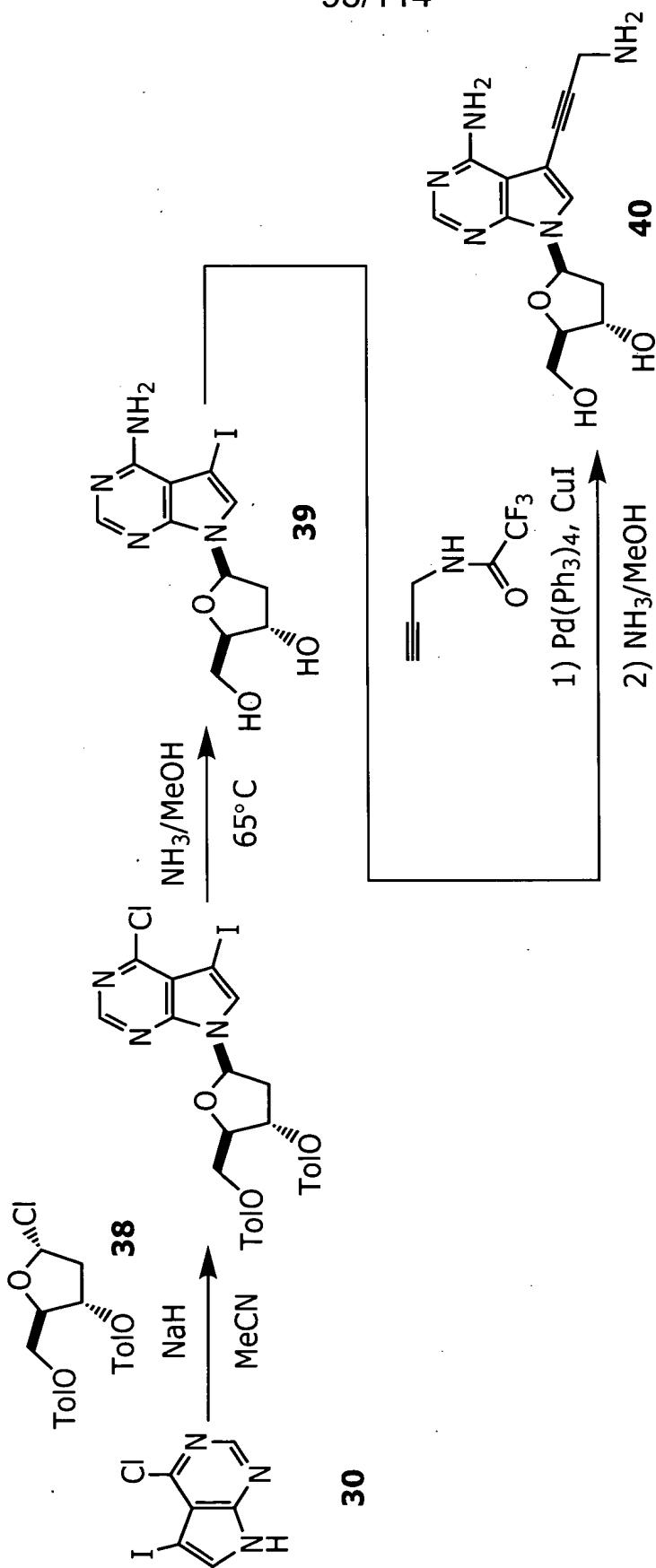


FIG. 71

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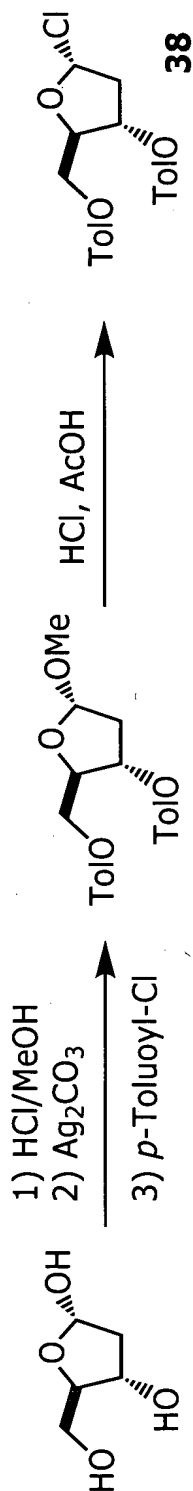
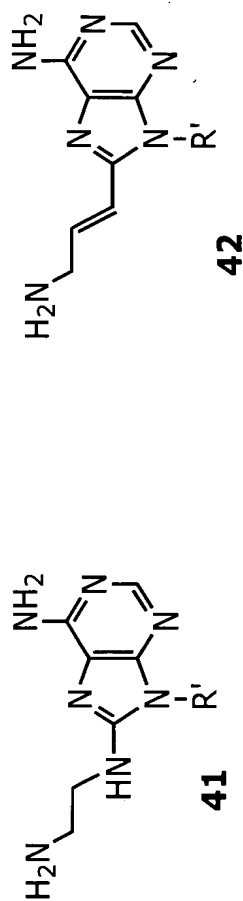
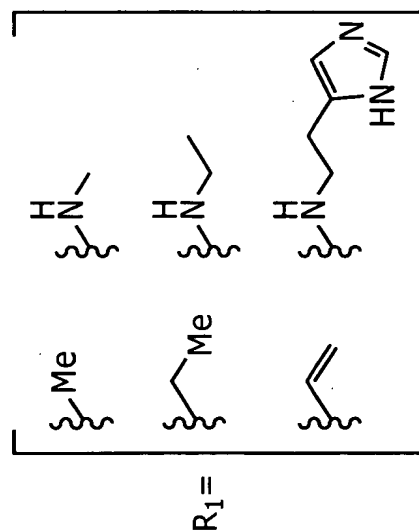


FIG. 72



R' = 2'-deoxyribose-5'-triphosphate

FIG. 73



a (R=Me): 1) HMDS, dioxane, 2) Me<sub>4</sub>Sn, Pd(PPh<sub>3</sub>)<sub>4</sub>, NMP, 3) K<sub>2</sub>CO<sub>3</sub>, MeOH  
b (R=Et): 1) HMDS, dioxane, 2) Et<sub>4</sub>Sn, Pd(PPh<sub>3</sub>)<sub>4</sub>, NMP, 3) K<sub>2</sub>CO<sub>3</sub>, MeOH  
c (R=CH<sub>2</sub>=CH): 1) HMDS, dioxane, 2) (CH<sub>2</sub>=CH)<sub>4</sub>Sn, Pd(PPh<sub>3</sub>)<sub>4</sub>, NMP,

**FIG. 74**

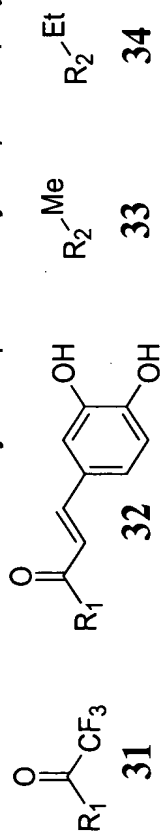
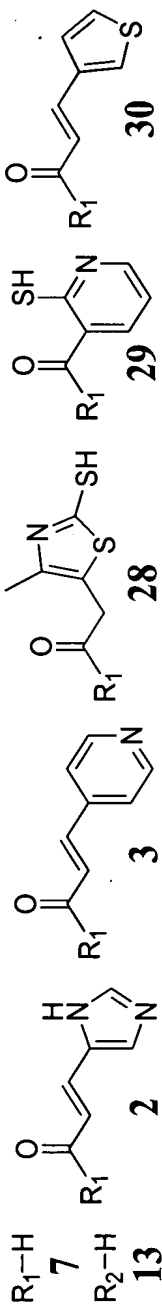
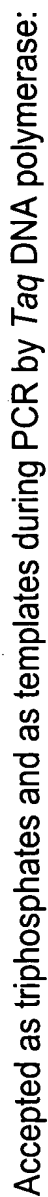


FIG. 75



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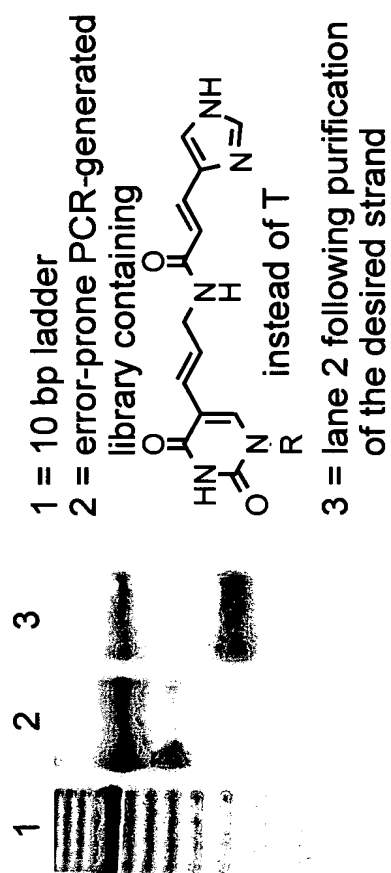


FIG. 76

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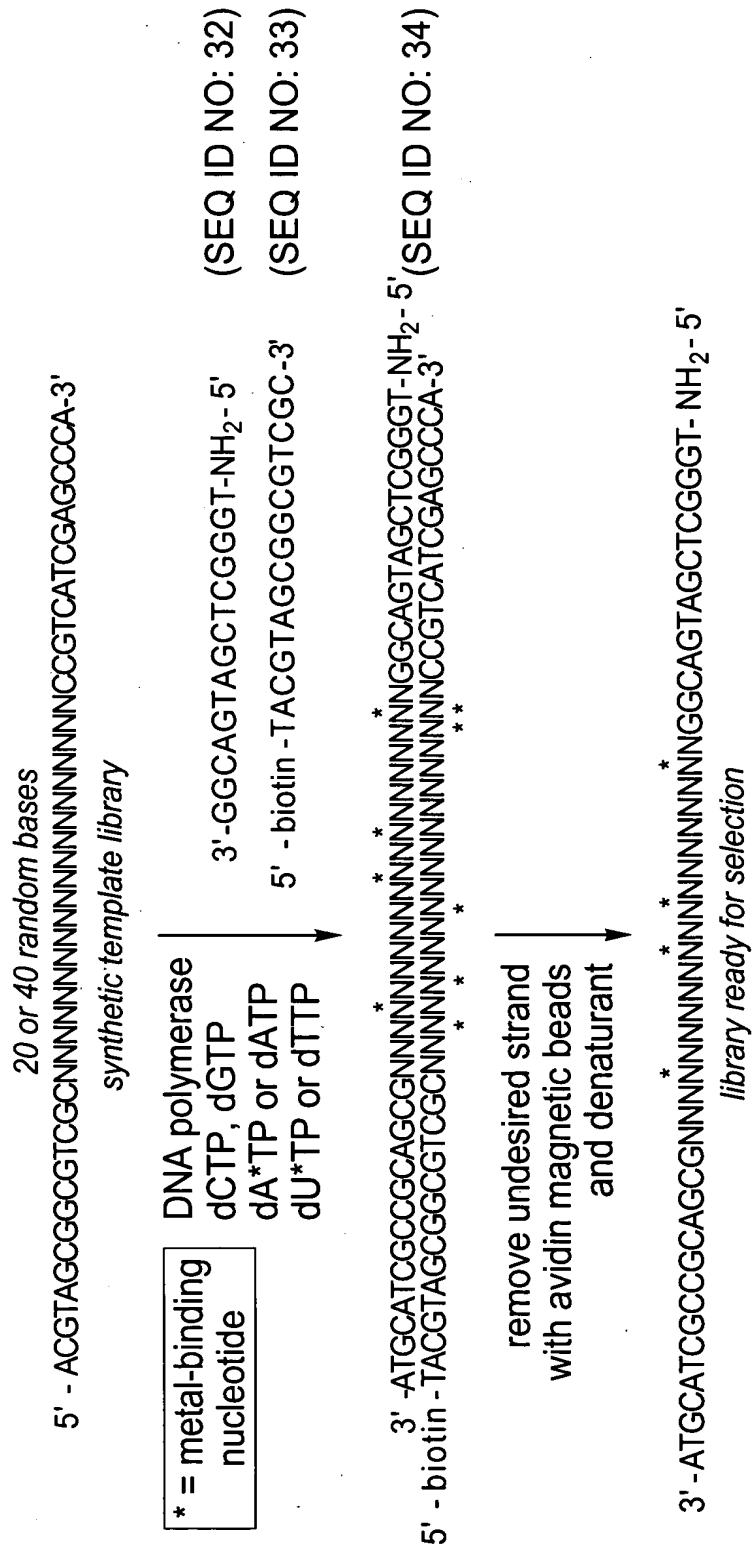


FIG. 77

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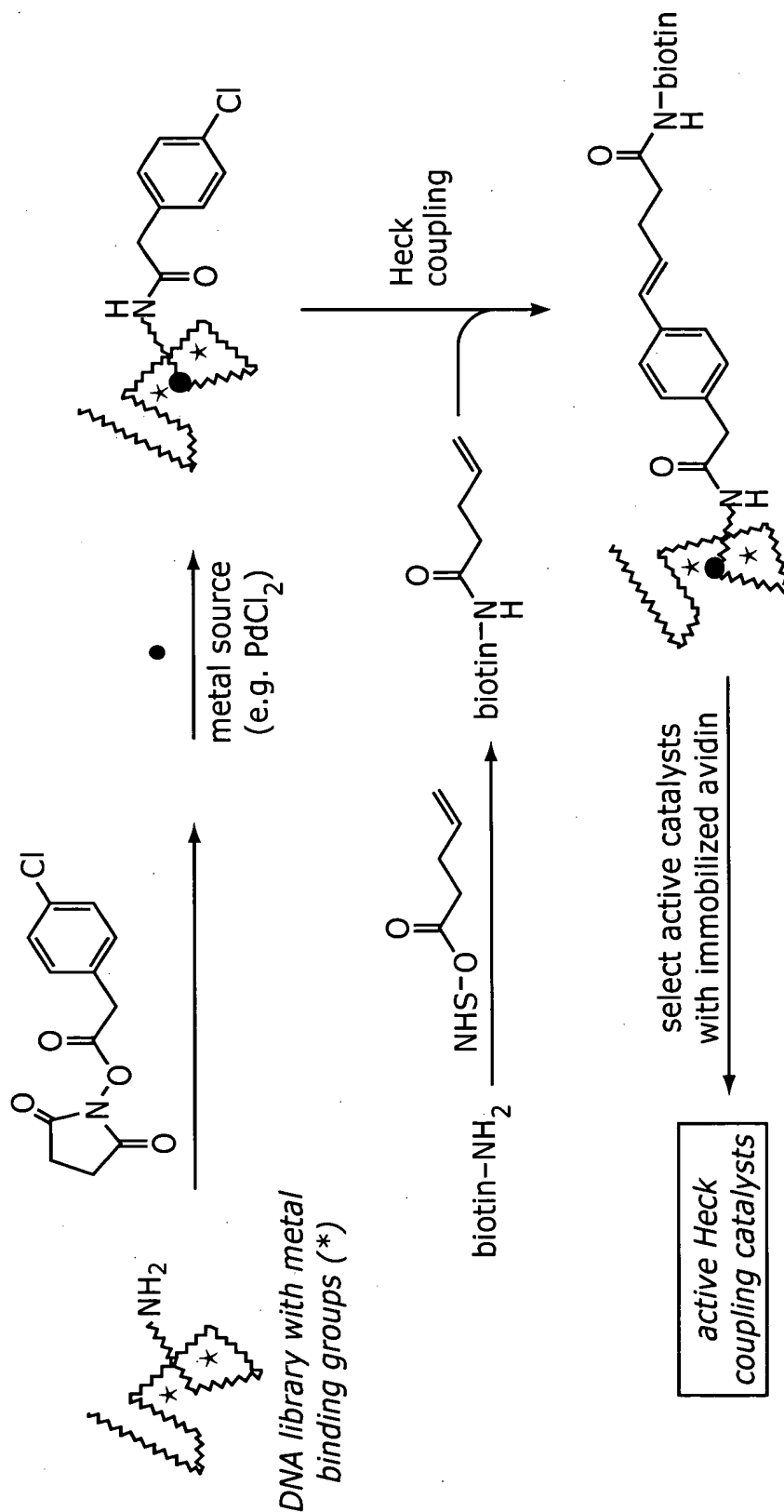


FIG. 78A

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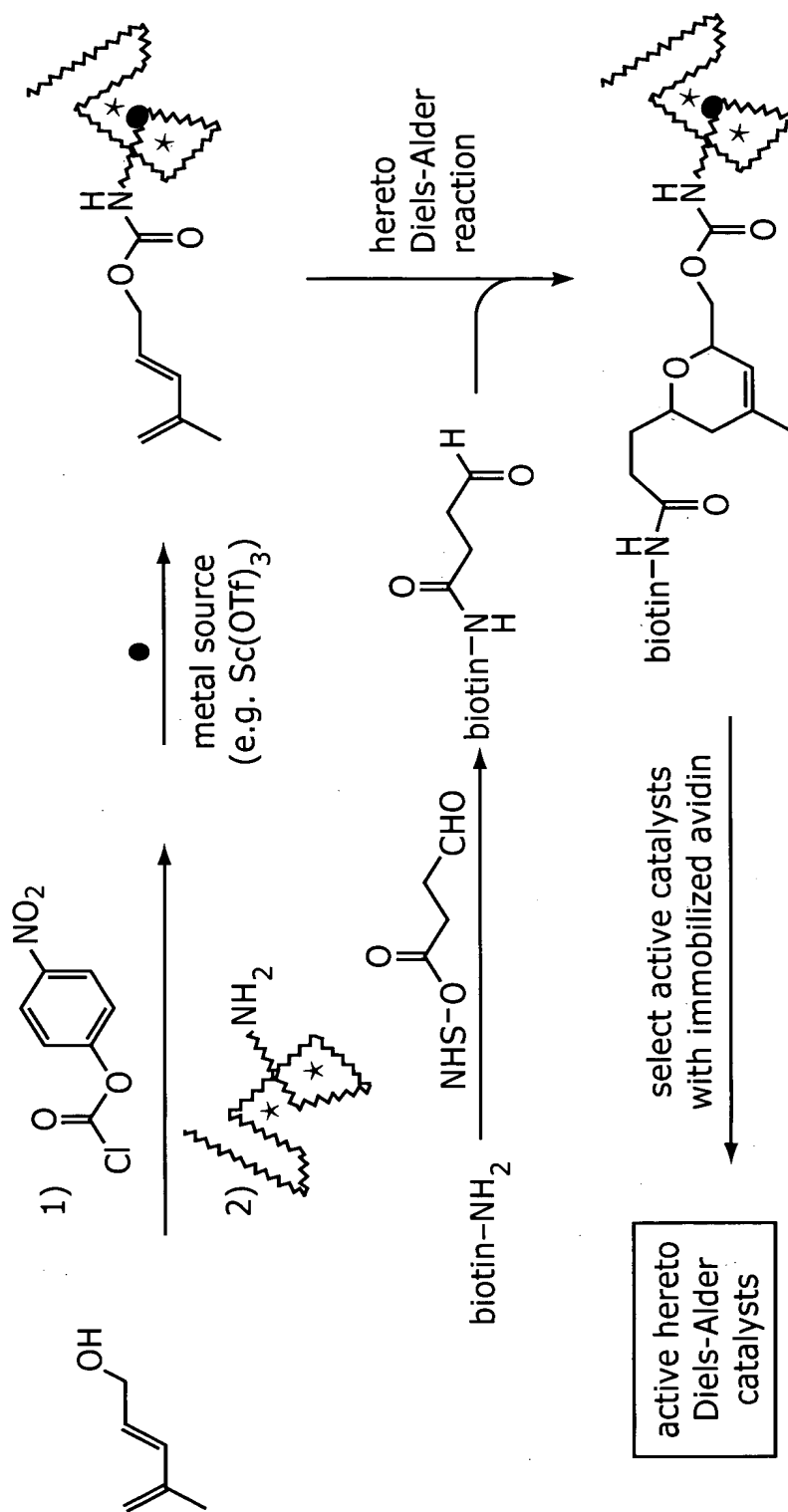


FIG. 78B

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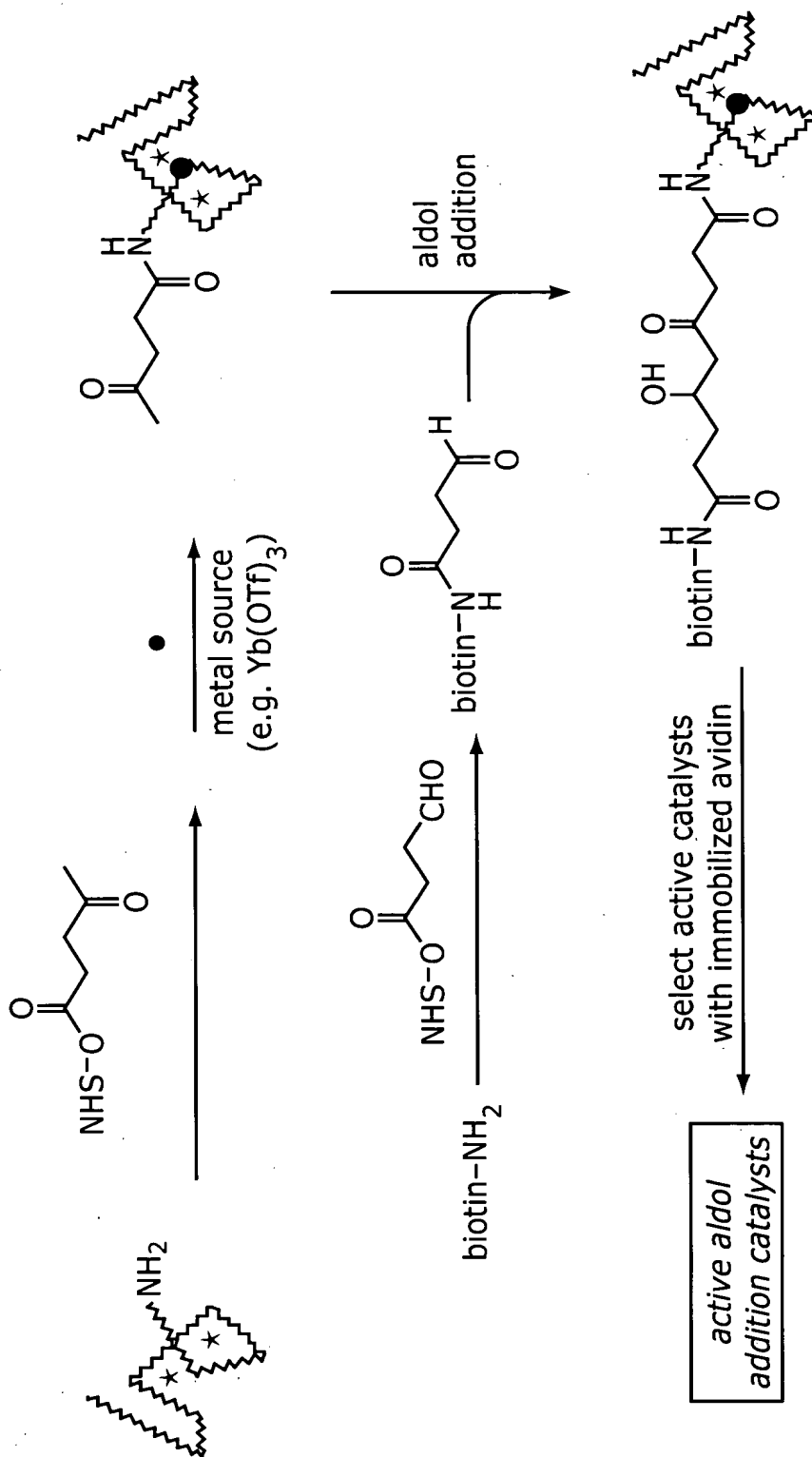
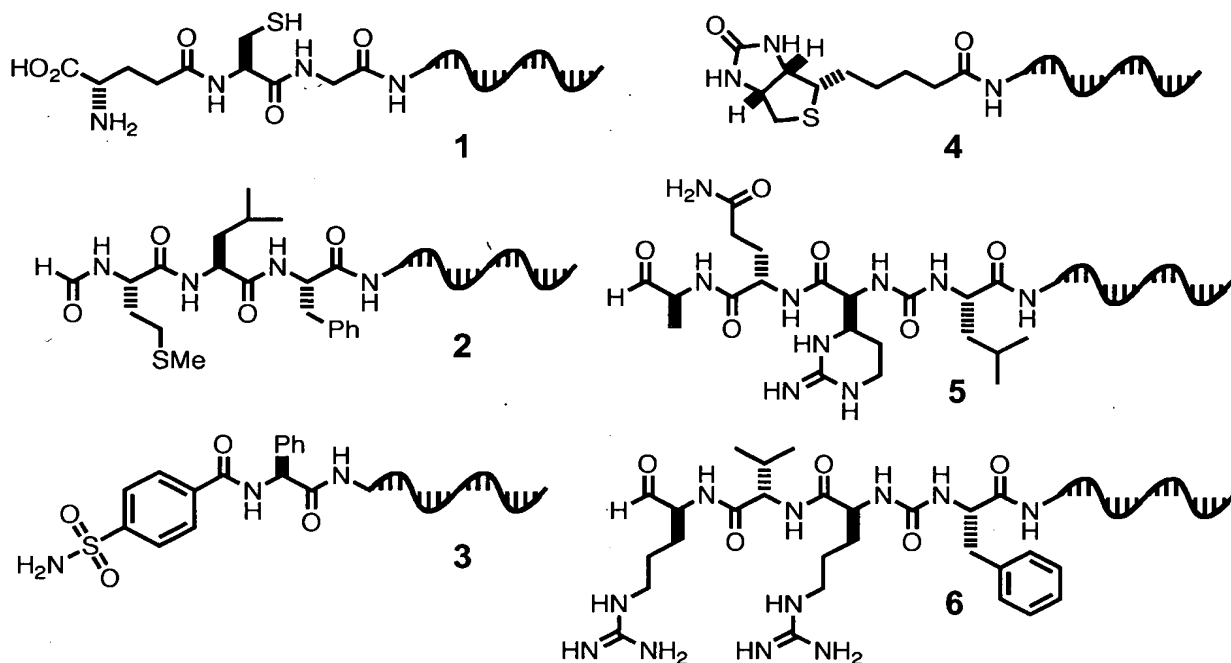


FIG. 78C

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| DNA-linked molecule | target protein            | predicted activity                | enrichment factor | sensitivity (mol) |
|---------------------|---------------------------|-----------------------------------|-------------------|-------------------|
| 1                   | glutathione S-transferase | $K_d = 10 \mu\text{M}$            | 2,500             | $10^{-20}$        |
| 3                   | carbonic anhydrase        | $K_d = 0.9 \text{ nM}$            | 330               | $10^{-20}$        |
| 4                   | streptavidin              | $K_d = 40 \text{ fM}$             | 4,400             | $10^{-18}$        |
| 5                   | papain                    | $\text{IC}_{50} = 14 \mu\text{M}$ | 64                | $10^{-16}$        |
| 5                   | chymotrypsin              | $\text{IC}_{50} = 290 \text{ nM}$ | 76                | $10^{-16}$        |
| 6                   | papain                    | $\text{IC}_{50} = 270 \text{ nM}$ | 98                | $10^{-18}$        |
| 6                   | trypsin                   | $K_d = 100 \text{ nM}$            | 125               | $10^{-17}$        |

FIG. 79

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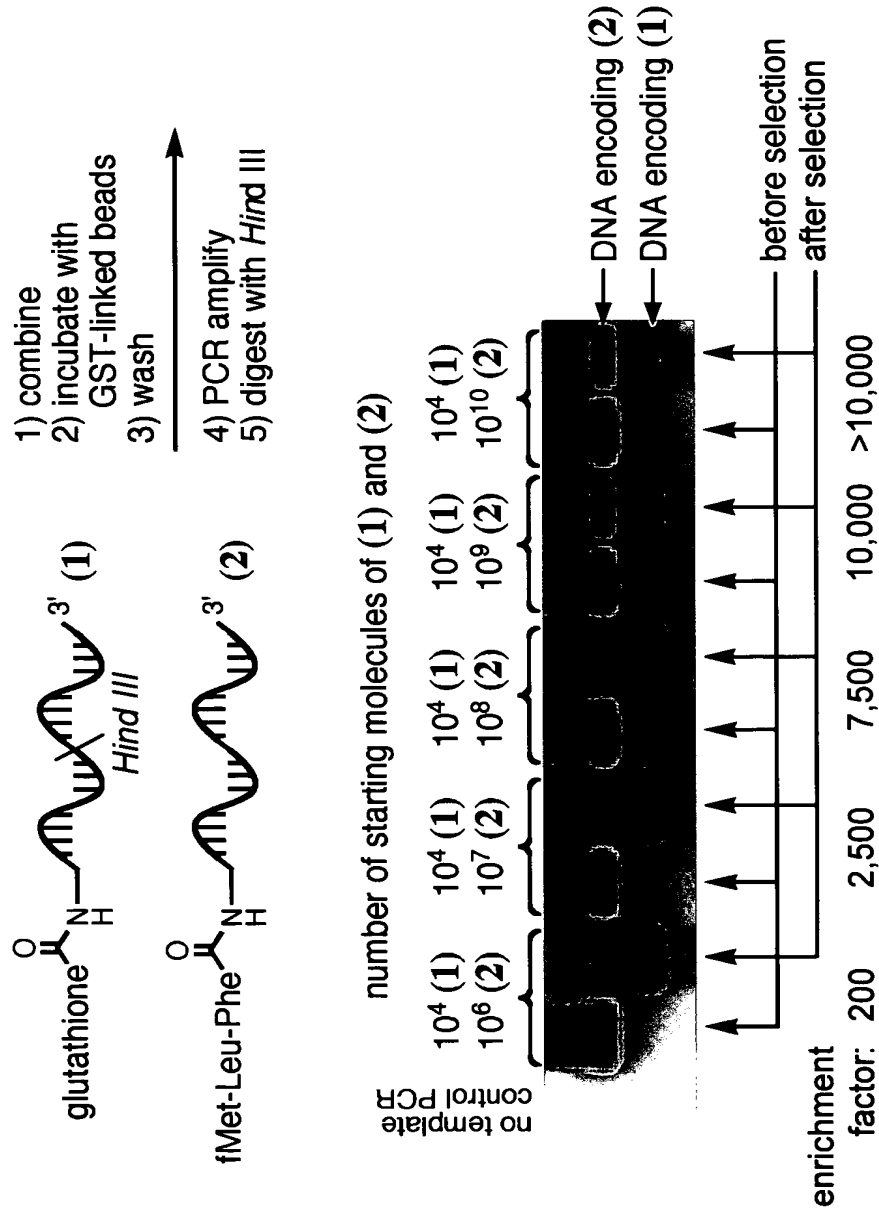


FIG. 80

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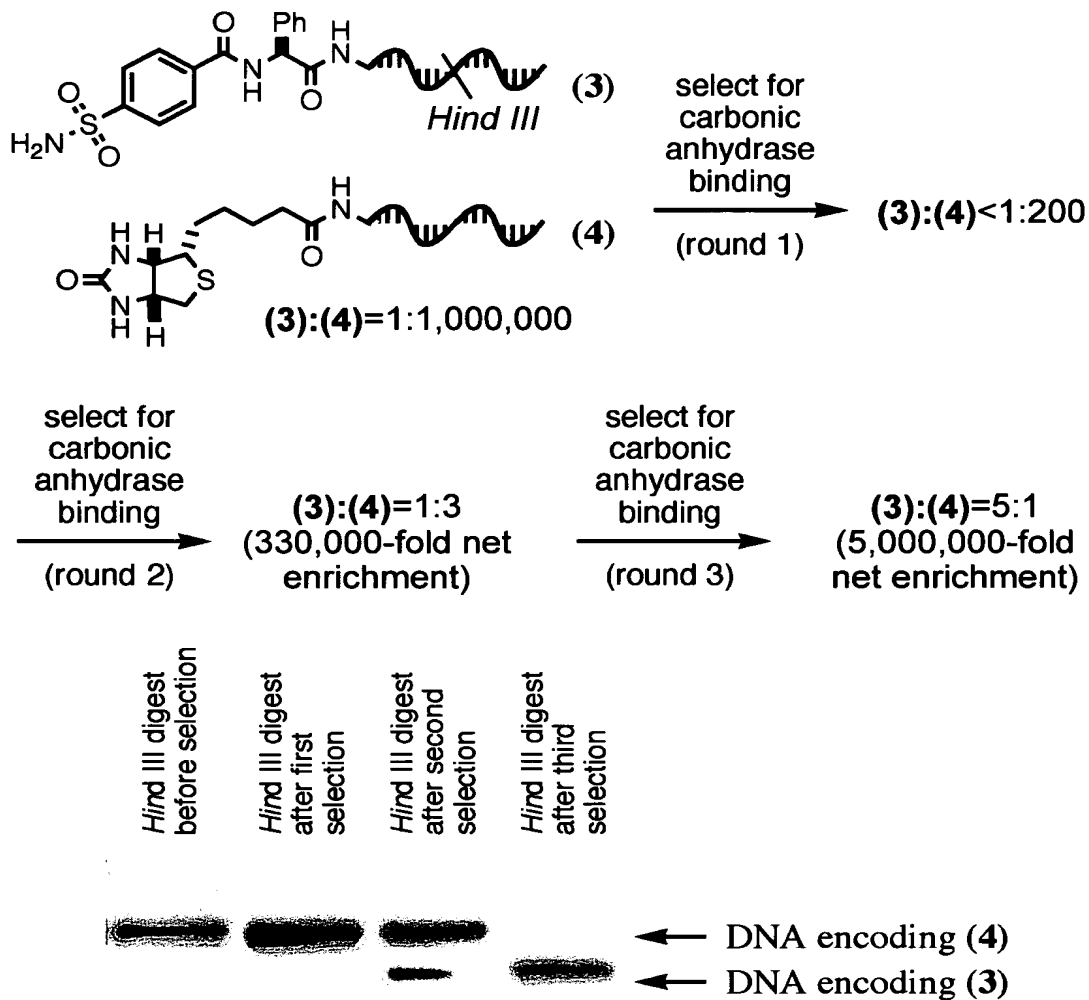
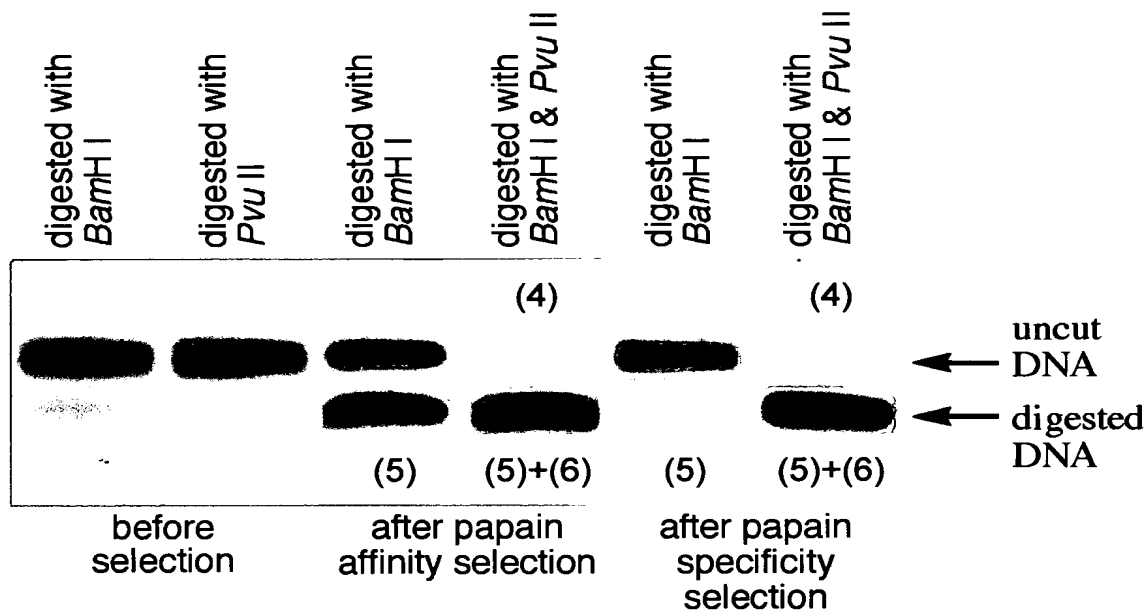
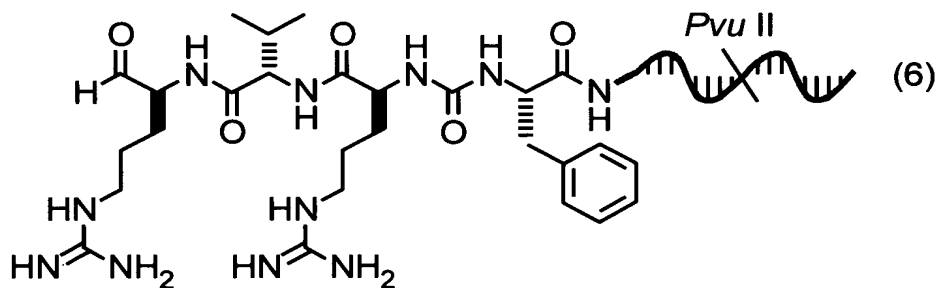
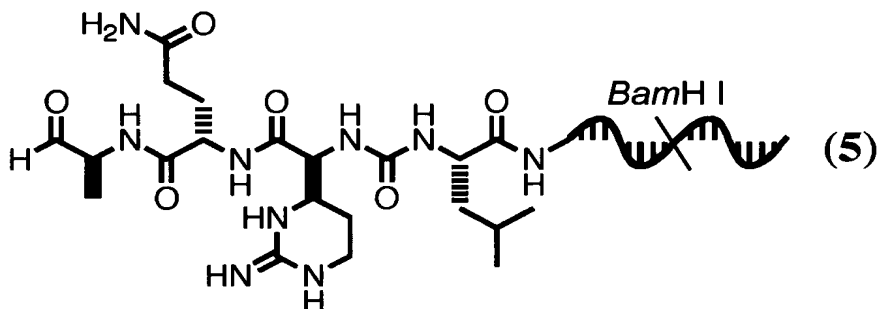
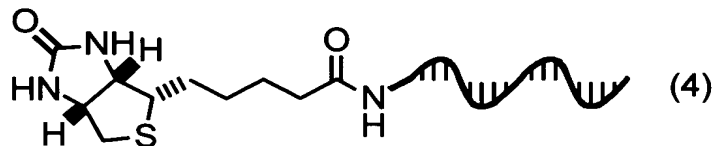


FIG. 81



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|     | IC <sub>50</sub> for<br>chymotrypsin <sup>10c</sup> | IC <sub>50</sub> for<br>papain <sup>10c</sup> | initial<br>ratio | ratio after<br>papain affinity<br>selection | ratio after papain<br>specificity<br>selection |
|-----|---|---|------------------|---|--|
| (4) | >500 $\mu$ M  | >500 $\mu$ M                                  | 24               | 1   | 1  |
| (5) | 0.29 $\mu$ M  | 14 $\mu$ M                                    | 4                | 12  | 1  |
| (6) | >500 $\mu$ M  | 0.27 $\mu$ M                                  | 1                | 12  | >10  |

FIG. 82

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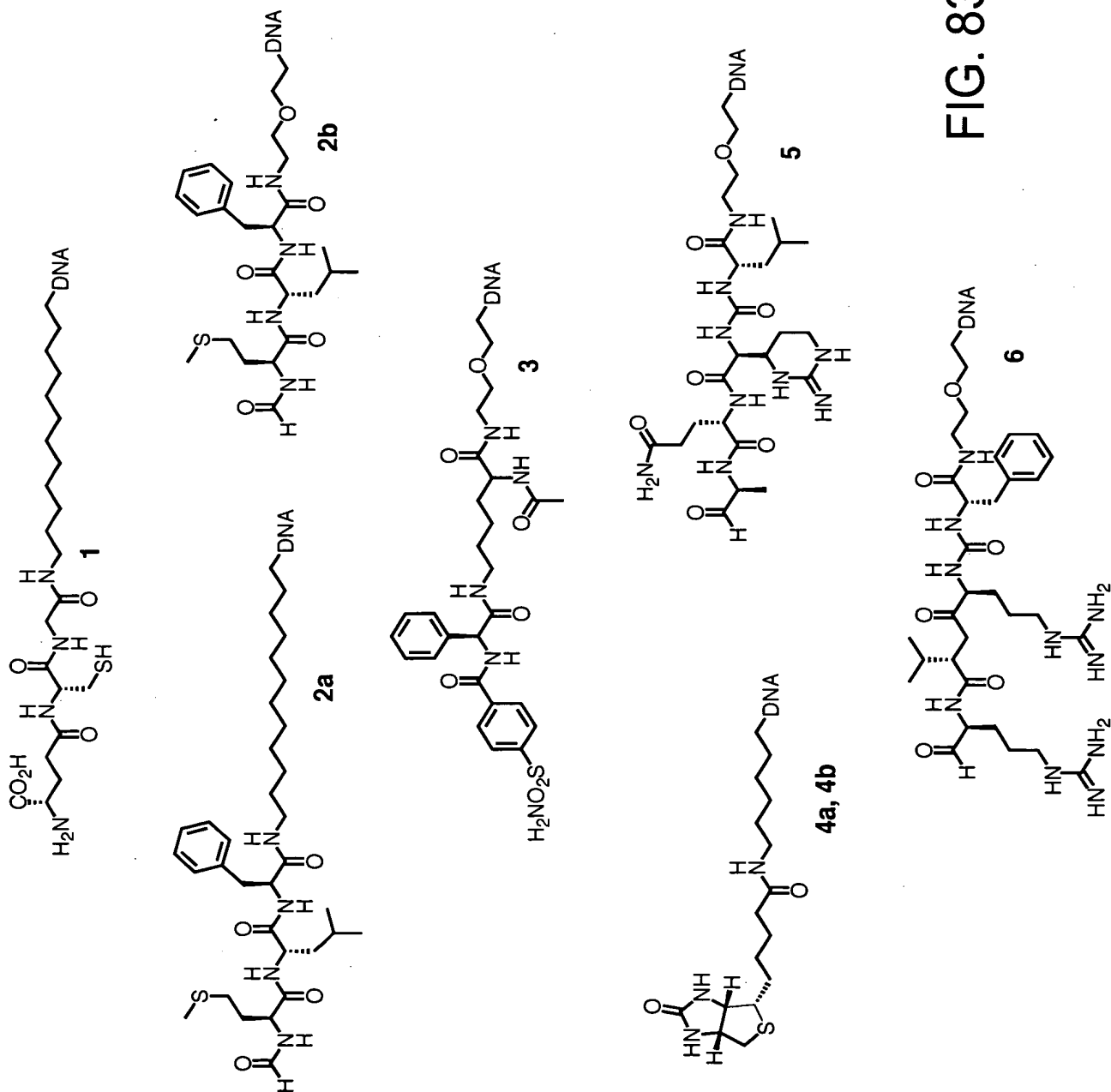


FIG. 83

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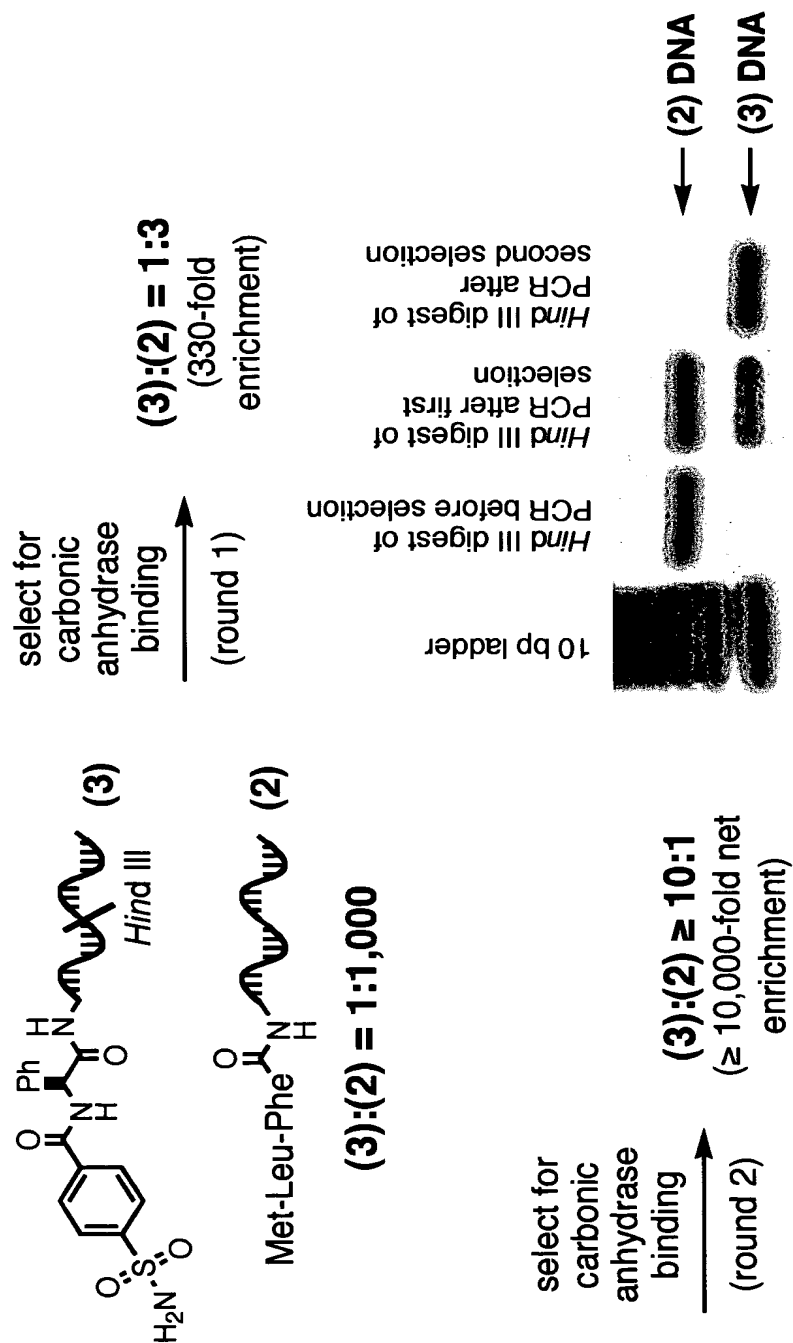


FIG. 84

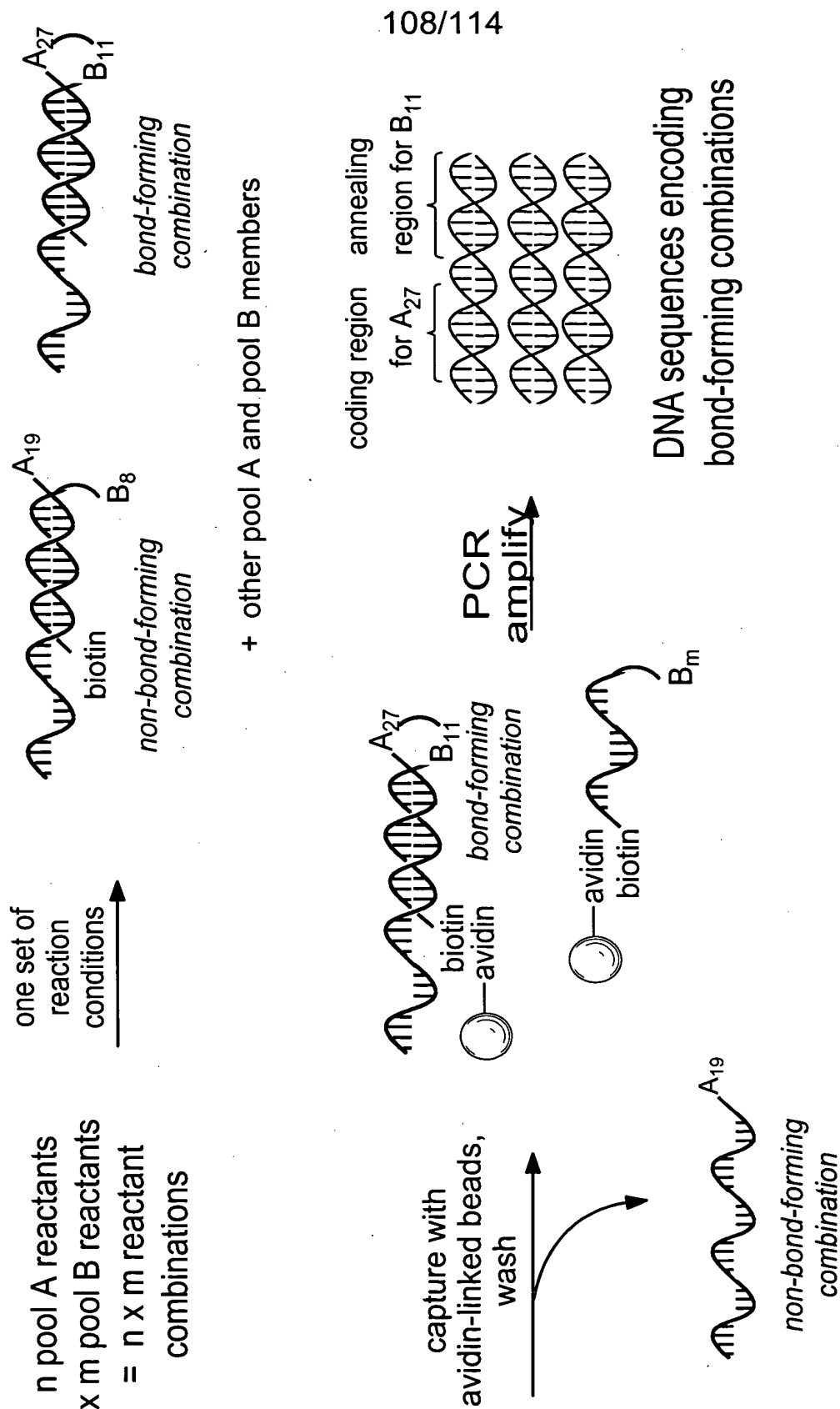


FIG. 85

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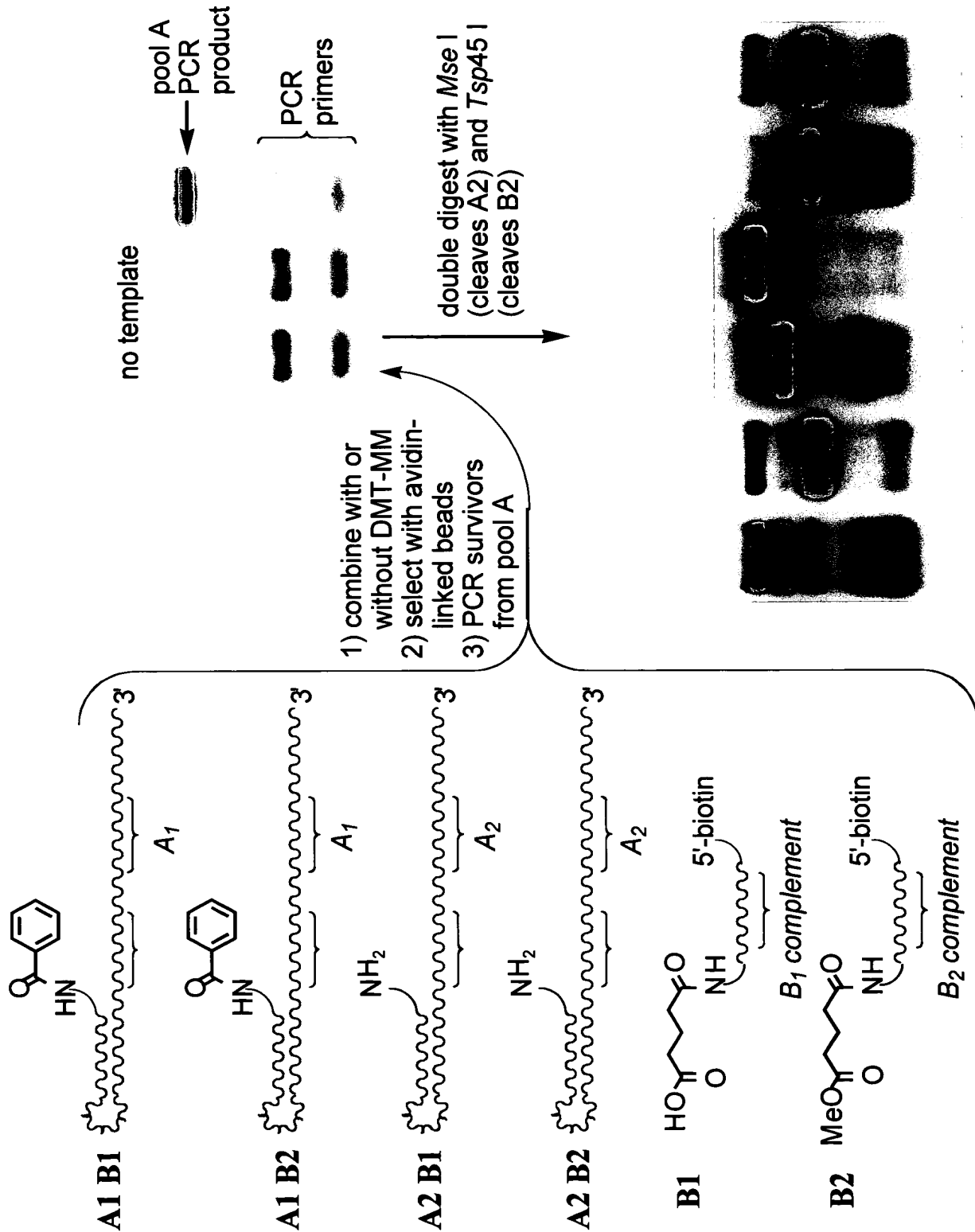
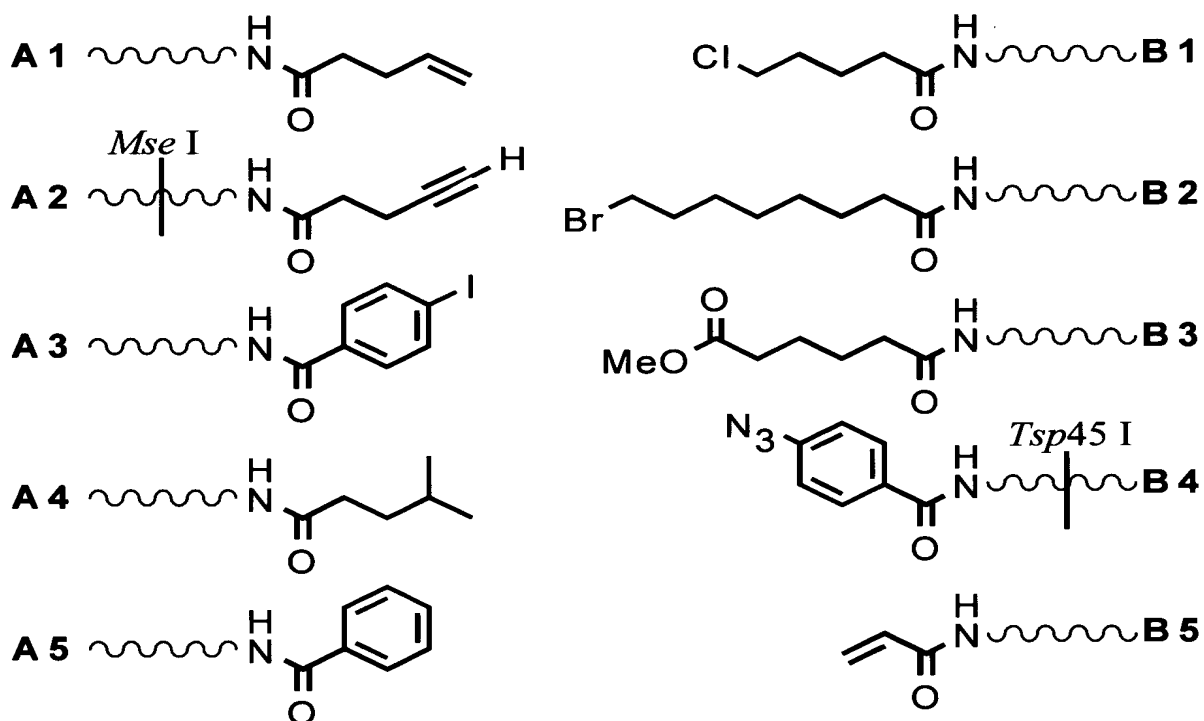


FIG. 86

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- 1) combine with or without  $\text{Cu}^+$
- 2) select with avidin-linked beads
- 3) PCR amplify survivors
- 4) double digest with *Mse* I (cleaves A2) & *Tsp45* I (cleaves B4)

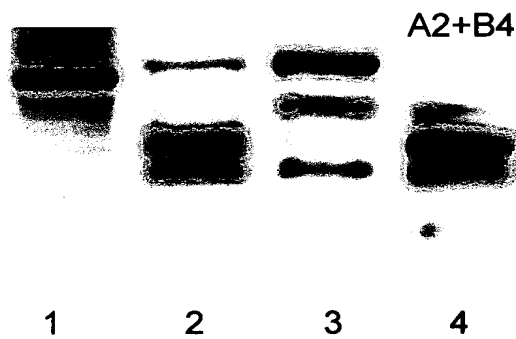


FIG. 87

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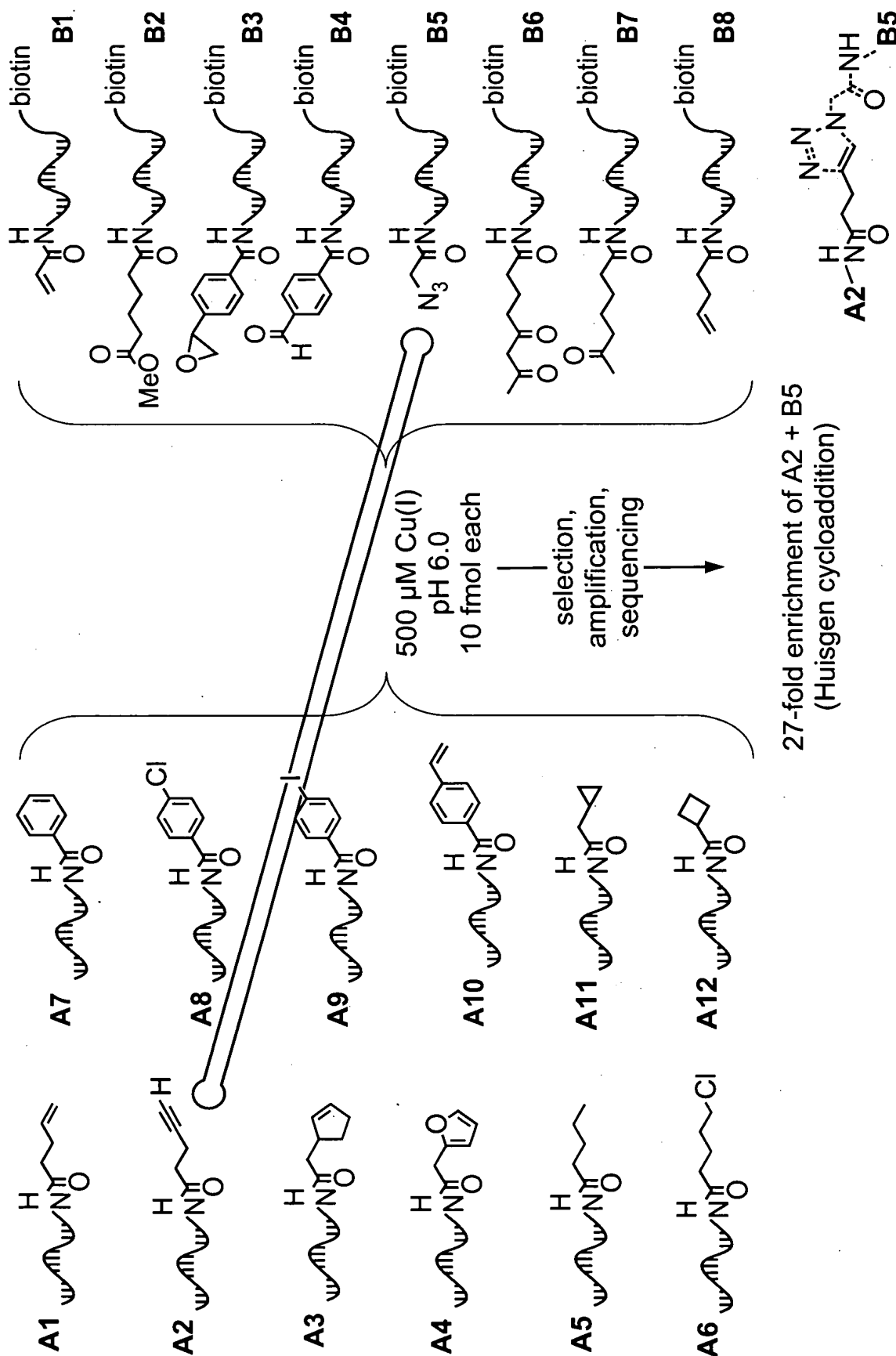
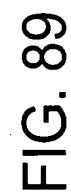


FIG. 88





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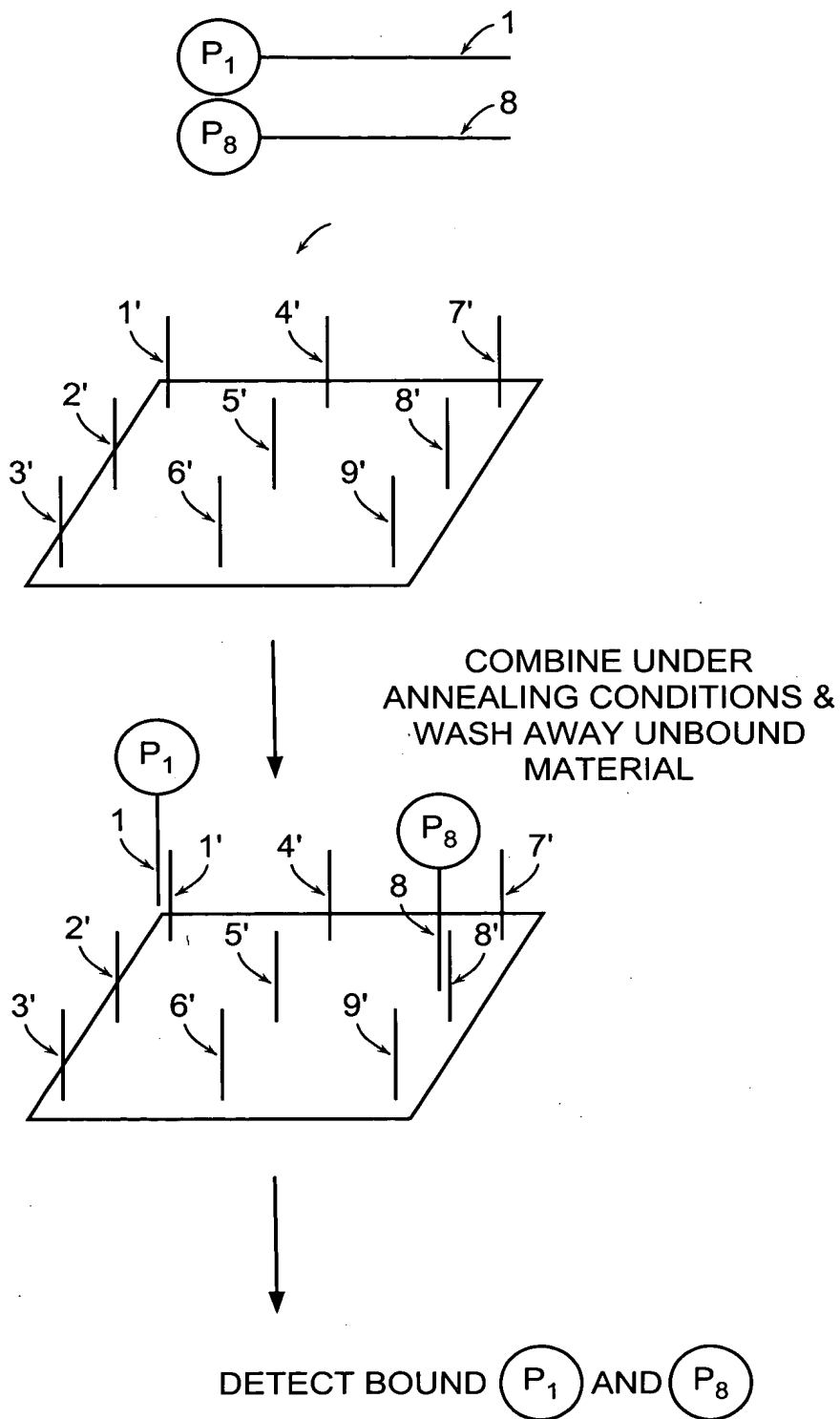


FIG. 90

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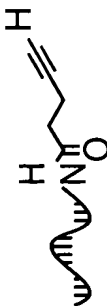
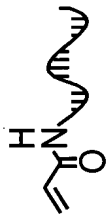
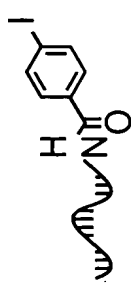
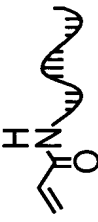
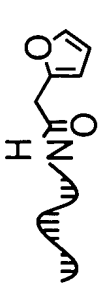
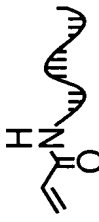
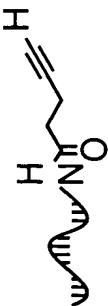
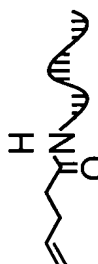
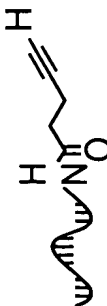
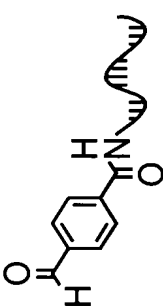
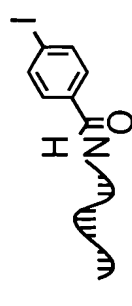
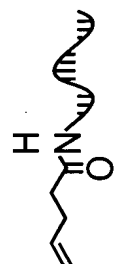
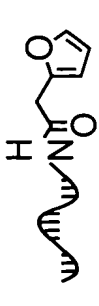
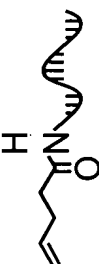
|   |   | ARRAY SIGNAL ÷<br>BACKGROUND  | DNA-TEMPLATED<br>REACTION YIELD |
|---|---|---|---------------------------------|
|    | + |              | 75-95%                          |
|    | + | (Heck)<br>   | 71-91%                          |
|    | + |              | 70-90%                          |
|    | + |              | 75-95%                          |
|   | + |             | 53-73%                          |
|  | + | (Heck)<br> | 57-77%                          |
|  | + |            | 75-95%                          |

FIG. 91